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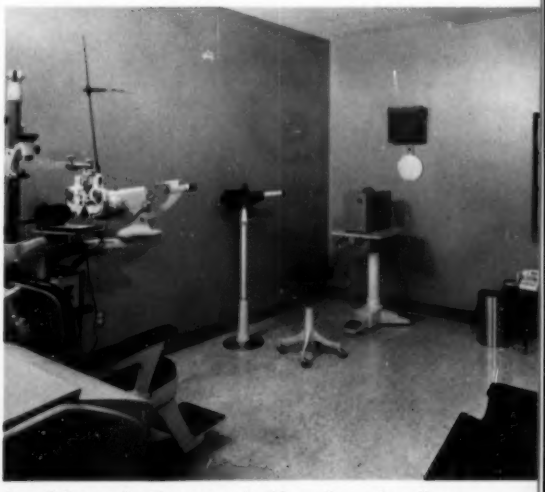

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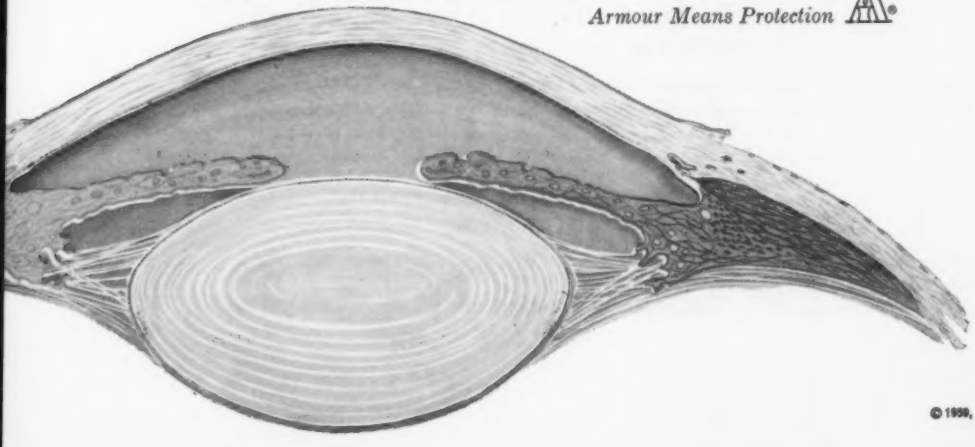

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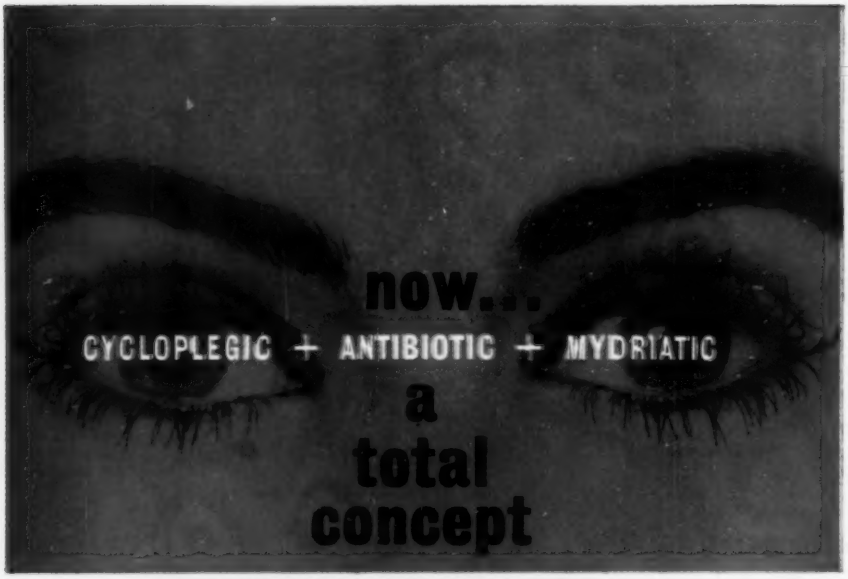

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References: 1. Miles, P. W.: Missouri Med. *56*:1243, 1959. 2. Sorsby, A.: Ann. Roy. Coll. Surgeons of England *22*:107, 1958. 3. Costner, A. N.: South. M. J. *48*:1192, 1955. 4. Rasgorshek, R. H., and McIntire, W. C.: Am. J. Ophth. *40*:34, 1955.

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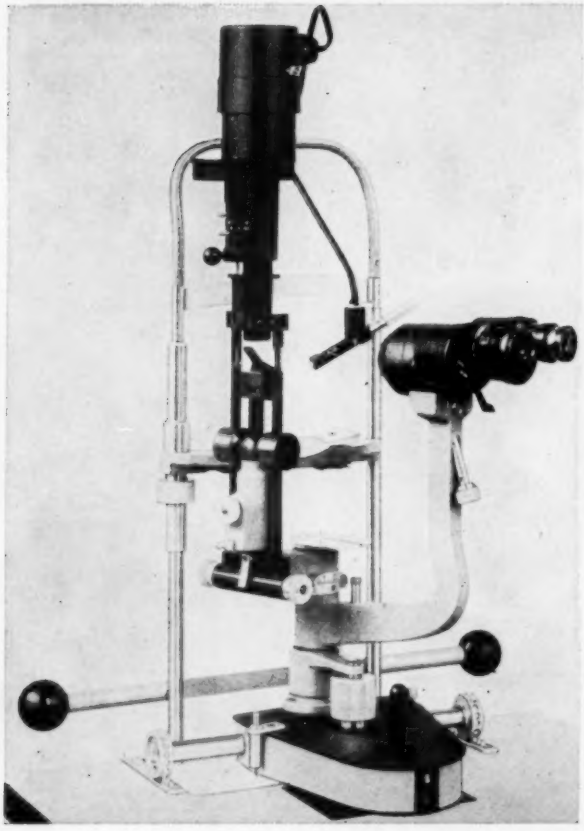

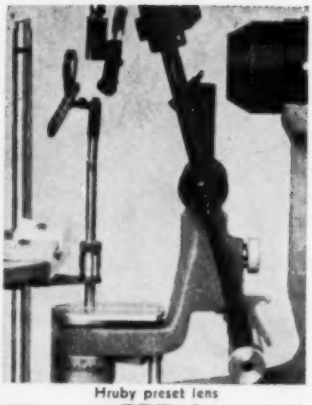

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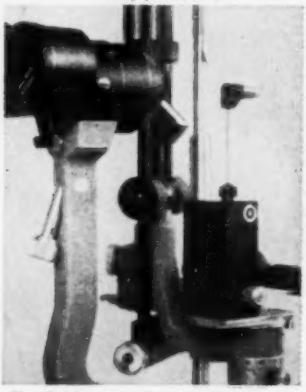

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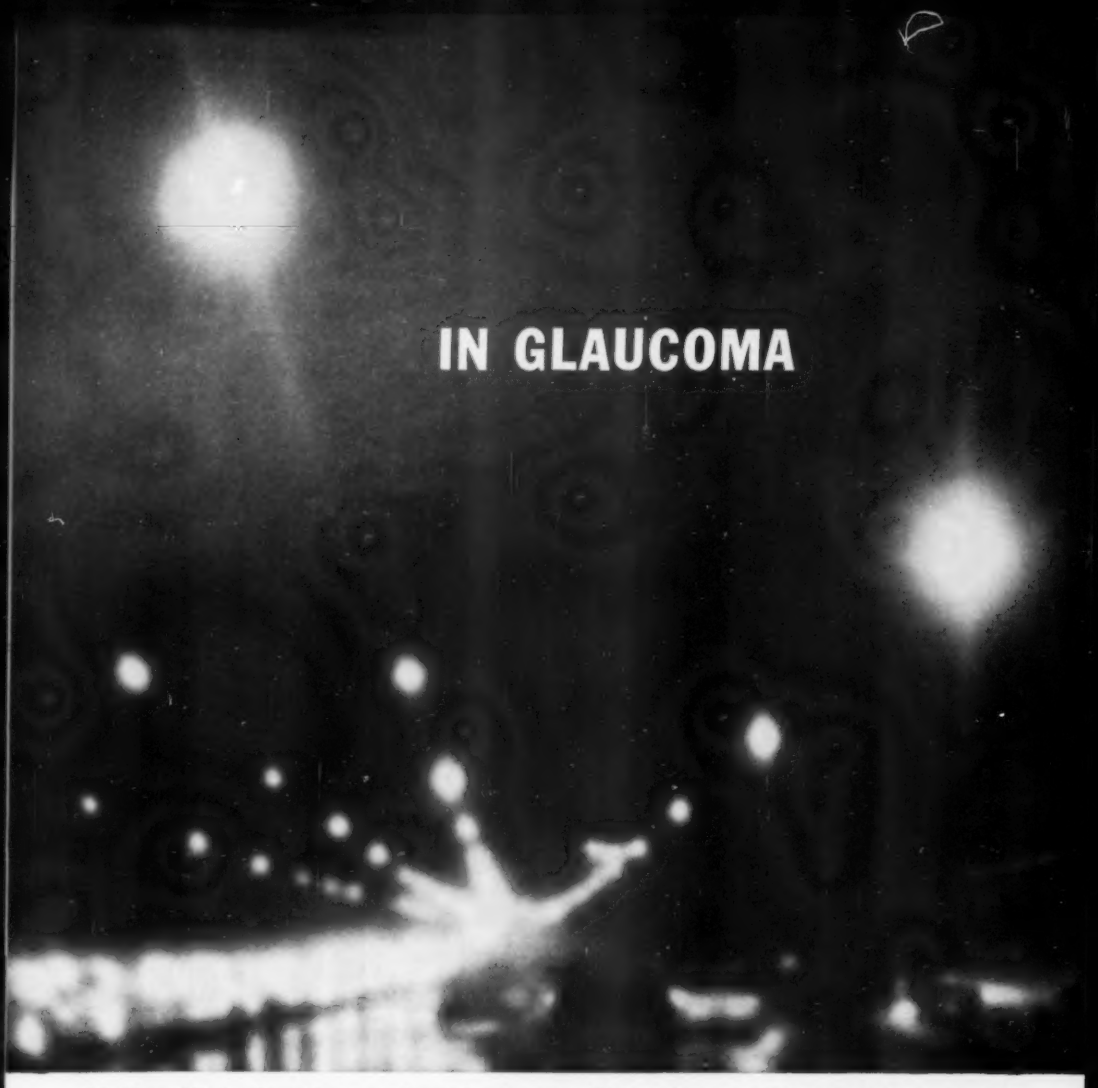

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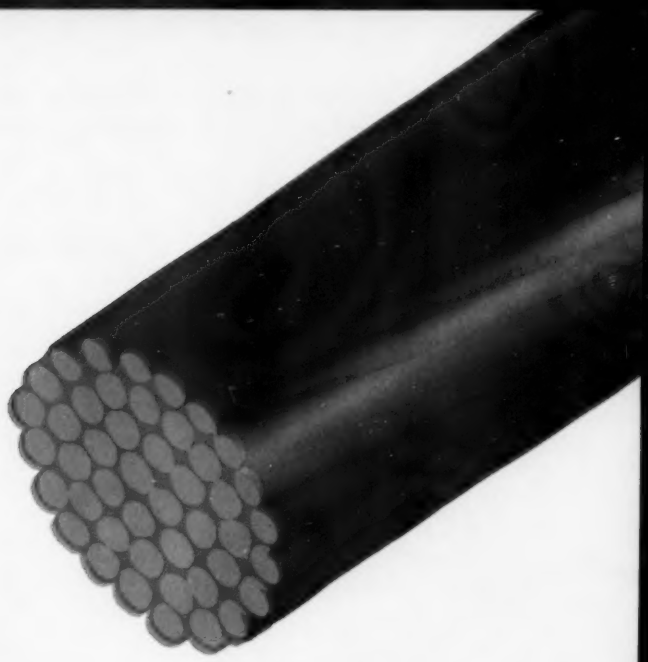

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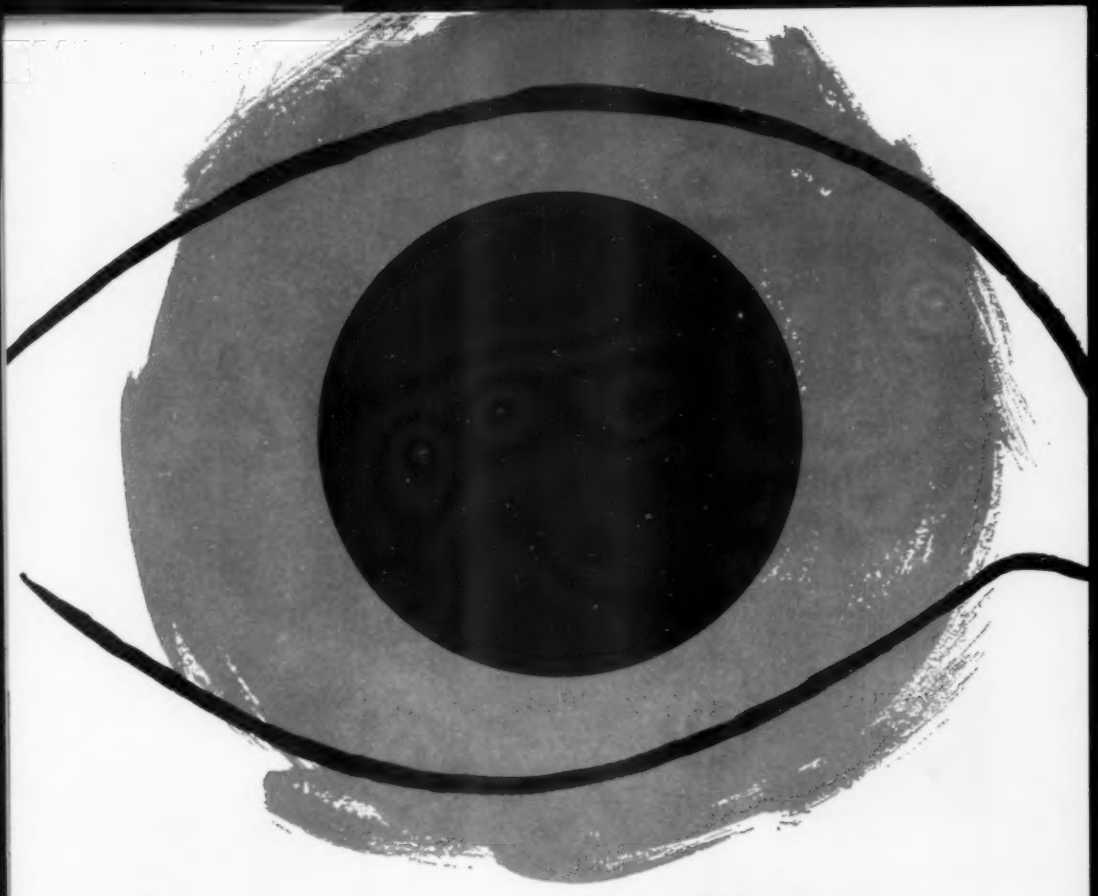

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0.5% ointment, tubes of ⅛ oz. (for the eye)

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This excellent line of English equipment is now at your disposal through us or through these C. & P. franchised dealers:

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Tibbs Physiologic Diplopia Reader

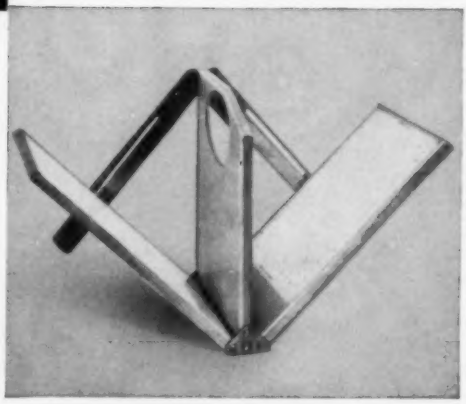
The Tibbs Physiologic Diplopia Reader is designed for patients with straight eyes. It is chiefly used for dissociation of accommodation and convergence, in accommodative strabismus, and for increasing area of comfort for reading when the middle third is either too far on the divergent or convergent side.

Stock No. 10915 Diplopia Reader, Tibbs Physiologic model, with Chart Boards, and complete instructions. $14.00

Tibbs Binocular Trainer

The Tibbs Binocular Trainer is designed for use in diagnosing and treating abnormal retinal correspondence; in breaking all types of suppression; and in developing vergence amplitudes.

Stock No. 10895 Binocular Trainer, Tibbs Model, with plastic target carriers and complete instructions. $23.50



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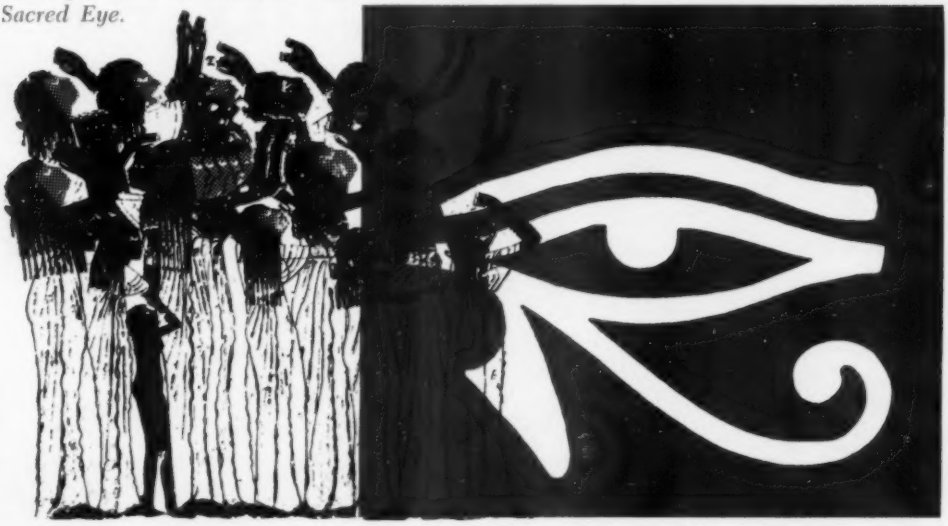
YESTERDAY... In ancient Egypt, when sight was threatened by the evil demons of disease, the patient sought relief by invoking the healing powers of UTCHAT—The Sacred Eye.



TODAY... IN SEVERE INFLAMMATORY AND ALLERGIC EYE DISEASE

new Prednefrin Forte® OPHTHALMIC SUSPENSION

PROVIDES UNEXCELLED EFFECTIVENESS FOR TOPICAL THERAPY

In many cases where other topical steriods have failed, PREDNEFRIN FORTE—the newest and most potent addition to the Prednefrin family—has demonstrated remarkable clinical effectiveness.[1]

PREDNEFRIN FORTE is specifically designed to treat the most severe anterior segment inflammatory disease effectively by virtue of its unique formula: prednisolone acetate *1.0%* for unexcelled counteraction of the disease process by its potent anti-inflammatory activity, plus . . . phenylephrine HCl 0.2% for rapid improvement of the eye's appearance and "feel" by its decongestant action.

PREDNEFRIN FORTE—presented in the special Allergan "solution-like" suspension—*offers new hope for saving sight whenever the functional integrity of the eye is threatened.*

TODAY—Whatever the degree of severity . . . whenever the diagnosis is ocular inflammation and/or allergy, you'll find a PREDNEFRIN specifically indicated.

SEVERITY	PREPARATION	INGREDIENT & STRENGTH	
		Prednisolone	Phenylephrine
Mild	Prednefrin Ophthalmic Suspension	0.12%	0.12%
Moderate	Prednefrin S Ophthalmic Solution	0.2%	0.12%
Severe	Prednefrin Forte Ophthalmic Suspension	1.0%	0.12%

Indications: All Prednefrin formulations are indicated in inflammatory and/or allergic disorders of the eyelids, conjunctiva, cornea, sclera and uveal tract—the degree of severity should determine the therapeutic choice.

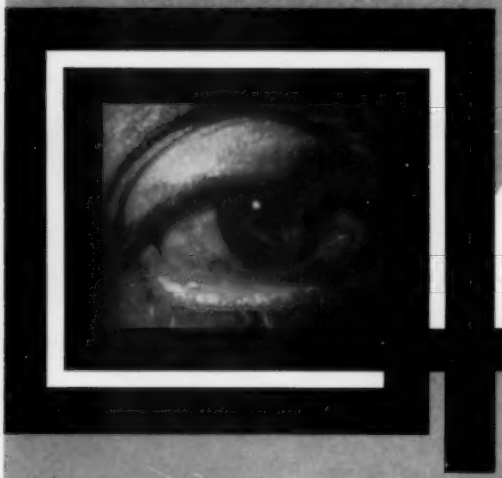
Dosage: 1 to 2 drops, two to four times daily. During the initial 24-48 hours, this dosage may be safely increased to 2 drops every hour.

Caution: Prednisolone is contraindicated in herpes simplex. If infection is present, appropriate anti-infective therapy should be employed.

Supply: Each member of the Prednefrin family is available in 5 cc. plastic dropper bottles, on prescription only.

Reference: 1 Albaugh, C.H.: Personal communication, 1959.

ALLERGAN PHARMACEUTICALS, INC., *Los Angeles 17, California*



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PILOCEL solutions provide the physician with a sterile, uniform accurately prepared miotic. PILOCEL spreads smoothly, with complete comfort to the patient. The METHULOSE* Vehicle assures uniform and prolonged contact with the eye — resulting in increased absorption — greater degree of miosis — less frequent application. Highly effective . . . well tolerated . . . convenient to use.

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systemic route to faster healing

controls inflammation, swelling and pain

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"Improvement with the use of Chymotrypsin (Chymar) noted in all cases within 24 hours."[1]

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"Chymotrypsin definitely shortens the course of ophthalmic inflammations and hastens the absorption of blood in the tissues."[2]

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"Two of three cases in this group showed definite improvement within six weeks."[1]

effective anti-inflammatory enzyme

CHYMAR Buccal—Crystallized chymotrypsin in a tablet formulated for buccal absorption. Bottles of 24 tablets. Enzymatic activity, 10,000 Armour Units per tablet.

CHYMAR Aqueous—Solution of crystallized chymotrypsin in sodium chloride injection for intramuscular use. Vials of 5 cc. Enzymatic activity, 5000 Armour Units per cc.

CHYMAR—Suspension of crystallized chymotrypsin in oil for intramuscular injection. Vials of 5 cc. Enzymatic activity, 5000 Armour Units per cc.

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1. Jenkins B. H.: J. M. A. Georgia *45*:431 (Oct.) 1956
2. Fullgrabe, E. A.: Ann. New York Acad. Sc. *68*:193 (Aug. 30) 1957.

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CHYMAR

EYES RIGHT

RIGHT because Gantrisin Ophthalmic Solution promptly and effectively controls a broad front of microorganisms, including such common pathogens as *Hemophilus influenzae* (Koch-Weeks). There is little likelihood of bacterial resistance emerging. **GANTRISIN OPHTHALMIC SOLUTION** is stable, sterile and isotonic, buffered at the pH of tears...no stinging, no burning. **RIGHT** in common external eye disorders, such as "pink eye" and nonspecific conjunctivitis, punctate and dendritic keratitis, superficial corneal ulcers, blepharitis; *also* in ocular trauma, for prophylaxis following surgery and after removal of foreign bodies.

Gantrisin Diethanolamine Ophthalmic Solution and Ointment contain 4% Gantrisin®—brand of sulfisoxazole.

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two highly effective topical miotics

in glaucoma... potent, prolonged control of intraocular pressure

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● long-acting—in glaucoma, one instillation daily is often sufficient, in strabismus, one instillation every two days to one week ● highly potent—may be effective when other agents fail ● two topical dosage forms—0.1% solution in peanut oil, in 5-cc. vials; 0.025% ointment, in 3.5 Gm. tubes

also available: **DARANIDE**® *for oral control of intraocular pressure, 50 mg. tablets*

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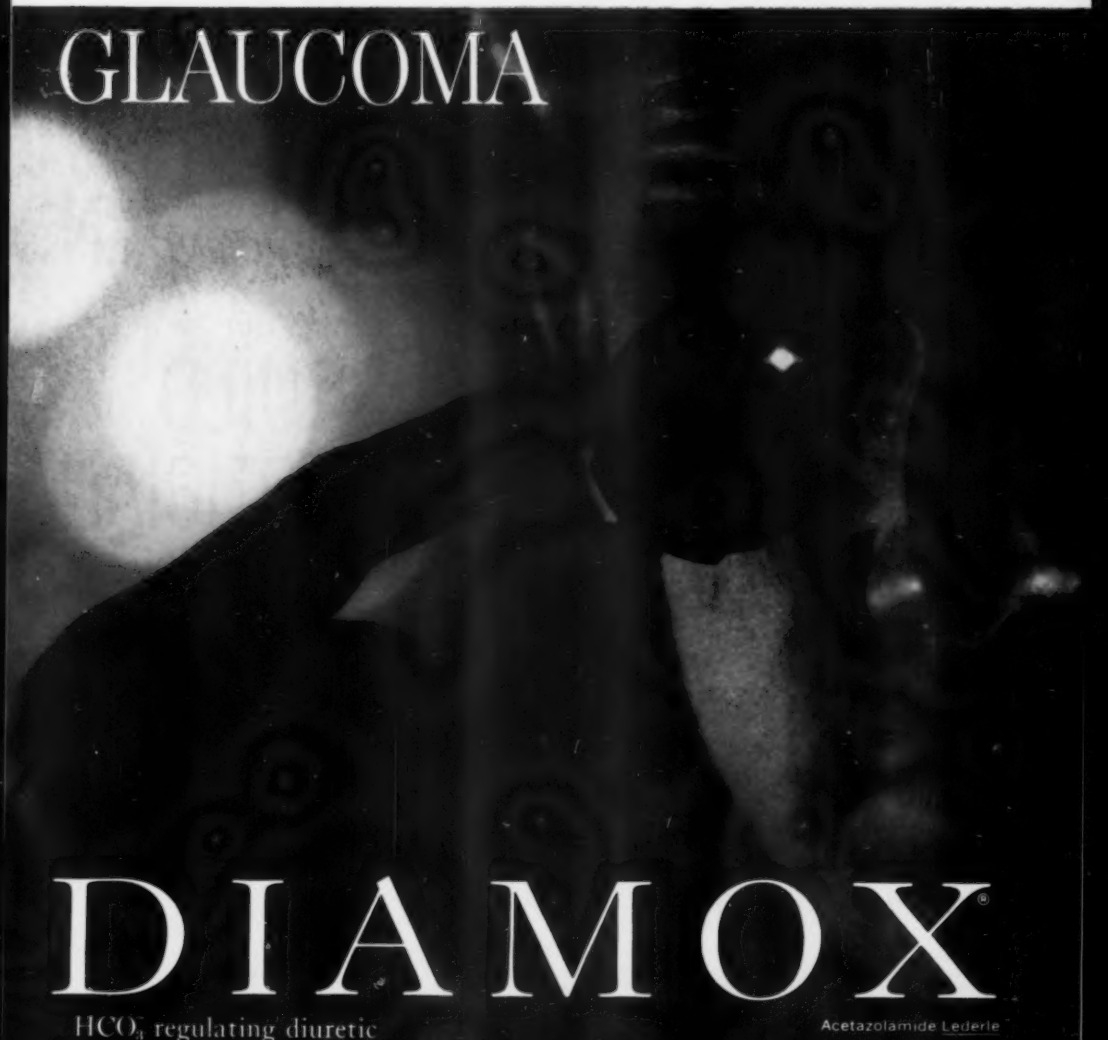
Suggested DIAMOX dosage for glaucoma: 250 mg. every four hours. In severe glaucomatous crises, the intravenous form may provide quicker reduction of global pressure.

Supplied: Scored tablets of 250 mg., and Vials of 500 mg. for parenteral use.

1. Venable, H. P.: J. Nat. M. A., 50:79, 1958.



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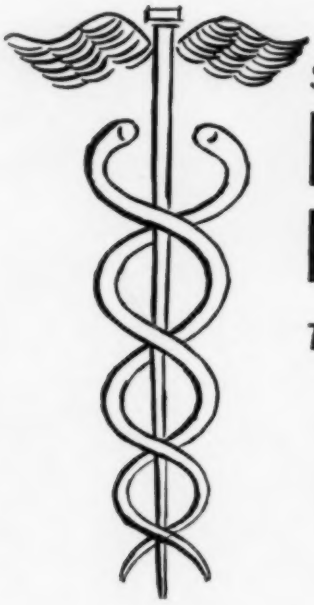
MEN AND WOMEN IN MANY PROFESSIONS & OCCUPATIONS
Present Special Eye Care Problems
THAT REQUIRE THE COMBINED SKILLS OF THE BEST TEAM



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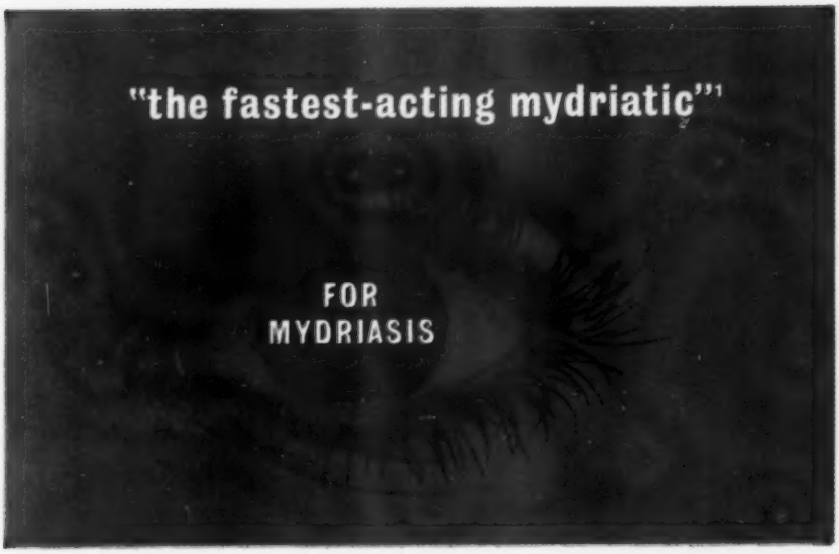

Rapid, profound mydriasis[1,2] with minimal cycloplegia . . . even in heavily pigmented irises. Excellent for ophthalmoscopic observation . . . resists the counteracting effects of bright lights. Quick return to normal—in 30 to 90 minutes with a miotic,[2] in 24 hours without a miotic.[3] Well-tolerated by children and elderly patients[1,4] . . . no evidence of side effects.[5]

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(CYCLOGYL® HCl 0.2% [cyclopentolate hydrochloride, Schieffelin], and phenylephrine hydrochloride 1.0% with PVP [polyvinylpyrrolidone] 3.0% in a sterile ophthalmic solution.)

Supplied in 7.5 ml. and 2 ml. dropper bottles.

Samples and literature available on request.

References: 1. Miles, P. W.: Missouri Med. *56*:1243, 1959. 2. Priestly, B. S.; Medine, M. M., and Phillips, C. C.: to be published. 3. Costner, A. N.: South. M. J. *48*:1192, 1955. 4. Rasgorshek, R. H., and McIntire, W. C.: Am. J. Ophth. *40*:34, 1955. 5. New and Nonofficial Drugs: J. B. Lippincott Company, 1958, p. 243.

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Of all plastic lens materials available, allyl ester hard resin plastic, called CR-39 is best suited for ophthalmic application. In respect to clarity and color freedom CR-39 is superb. Enduron lenses are precision-cast from CR-39. They have their own system of computations for corrected curves based on marginal astigmatic variation.

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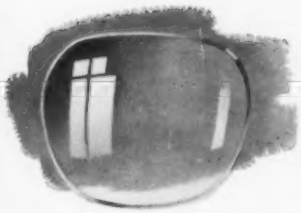
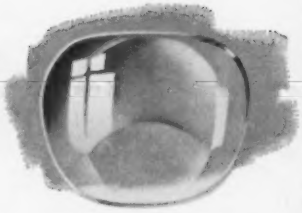


Enduron Single Vision

Enduron Round-Seg Bifocal



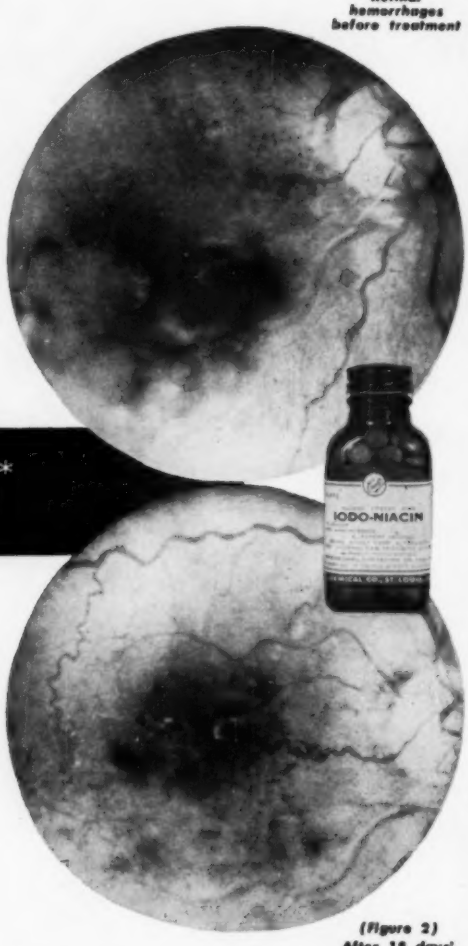
Enduron High Plus Lenticular (one of three styles depending on power)

retinal hemorrhages absorbed

with use of

IODO-NIACIN*

(Figure 1)
Retinal hemorrhages before treatment



(Figure 2)
After 18 days' treatment with Iodo-Niacin

NO IODISM

As shown by retinal photography, rapid absorption of retinal hemorrhages follows use of IODO-NIACIN. These results have been established in a series of 22 cases, 12 of retinal and 10 of vitreous hemorrhages.[1]

IODO-NIACIN Tablets contain potassium iodide 135 mg. (2¼ gr.) and niacinamide hydroiodide 25 mg. (⅜ gr.). The dosage used was 1 tablet three times a day. For greater effect this dosage may be doubled.

IODO-NIACIN may be administered in full dosage for a year or longer without any iodism or ill effect.[2]

In emergencies, for rapid and intensive action, IODO NIACIN Ampuls may be used intramuscularly or intravenously.[3] IODO-NIACIN Tablets are supplied in bottles of 100. Slosol coated pink. Ampuls 5 cc. boxes of 10.

1. *Am. J. Ophth.* 42:771, 1956.
2. *Am. J. Digest Dis.* 22:5, 1955.
3. *Med. Times* 84:741, 1956.

*U.S. Patent Pending

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clear lenses (not tinted) absorb 90% of the ultraviolet rays normally entering the eyes

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1960 COMPREHENSIVE CONTACT LENS SEMINARS
THREE-DAY SEMINARS / LENS ADJUSTMENT SEMINARS

TIME: All seminars will be held from 10 a.m. to 5 p.m. daily.

THREE-DAY SEMINAR: A comprehensive course of study designed to provide information and practical knowledge that can assist you in successfully fitting contact lenses. The latest techniques and developments will be presented such as fitting SPHERCON®, Bi-Curve and Tri-Curve lenses; the use of the new TORCON* lens in fitting unusual astigmia cases; the techniques of fitting BICON®, de Carle, and C. B. bifocal contact lenses; TELECON*, a recently introduced subnormal vision aid; Photo-Electronic-Keratoscopy (PEK*), its theory and use; CONTA-SONICS*, an invaluable aid to the practitioner.

To gain practical experience, each practitioner who registers for this course will receive a personal pair of contact lenses, which will be fitted in class. Your K-readings and Rx must be included with your registration so that your lenses can be processed prior to course date.

ONE-DAY LENS ADJUSTMENT SEMINAR: Provides the basic theory and practice required to perform all contact lens adjustments. This course to include: The CON-LISH* process of uniform edge finishing; methods of applying a CN bevel; grinding, polishing, and blending of intermediate and peripheral curves. The fundamentals of proper lens inspection will be fully demonstrated. Skill in lens inspection will enable you to objectively verify each lens adjustment you make.

SPRING 1960 SCHEDULE OF COMPREHENSIVE SEMINARS

Three-Day Seminars	Lens Adjustment Seminars	City and State	Hotel
February 23-24-25	February 26	Memphis, Tennessee	Peabody
March 1-2-3	March 4	Detroit, Michigan	Statler
March 8-9-10	March 11	Washington, D. C.	Statler
March 15-16-17	March 18	Salt Lake City, Utah	Utah
March 22-23-24	March 25	New York, New York	‡Vision Center
April 5-6-7	April 8	Los Angeles, California	Ambassador
April 12-13-14	April 15	Phoenix, Arizona	Westward Ho
April 19-20-21	April 22	Miami, Florida	McAllister
April 26-27-28	April 29	New Orleans, Louisiana	Jung
May 3-4-5	May 6	St. Louis, Missouri	Coronado
May 10-11-12	May 13	Dallas, Texas	Sheraton
May 24-25-26	May 27	Boston, Massachusetts	Sheraton-Plaza
June 7-8-9	June 10	Montreal, Quebec	Queen Elizabeth
June 14-15-16	June 17	Philadelphia, Pennsylvania	Sheraton
June 21-22-23	June 24	Denver, Colorado	Brown Palace

*Trademark

‡This Seminar will be held at the Wesley/Jessen Contact Lens Company, Vision Building, 635 Madison Ave., New York 22, N.Y.

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Please mail to THE PLASTIC CONTACT LENS COMPANY, 5 South Wabash Avenue, Chicago 3, Illinois. A $25.00 DEPOSIT IS REQUIRED WITH ALL REGISTRATIONS. CHECK THE SEMINAR YOU DESIRE TO ATTEND:

Note: If registering for the Three-Day Course, be sure to include your K-readings and Rx so we may process your lenses prior to seminar date.

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☐ Enclosed is my registration check for $65.00 for the Three-Day Contact Lens Seminar.

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(Date of Seminar) _____ City _____

Name _____

Your Mailing Address _____

City _____ Zone _____ State _____

RECORD K-READINGS AND YOUR RX HERE:

K-Readings: O. D. _____ O. S. _____

Refraction: O. D. _____ O. S. _____

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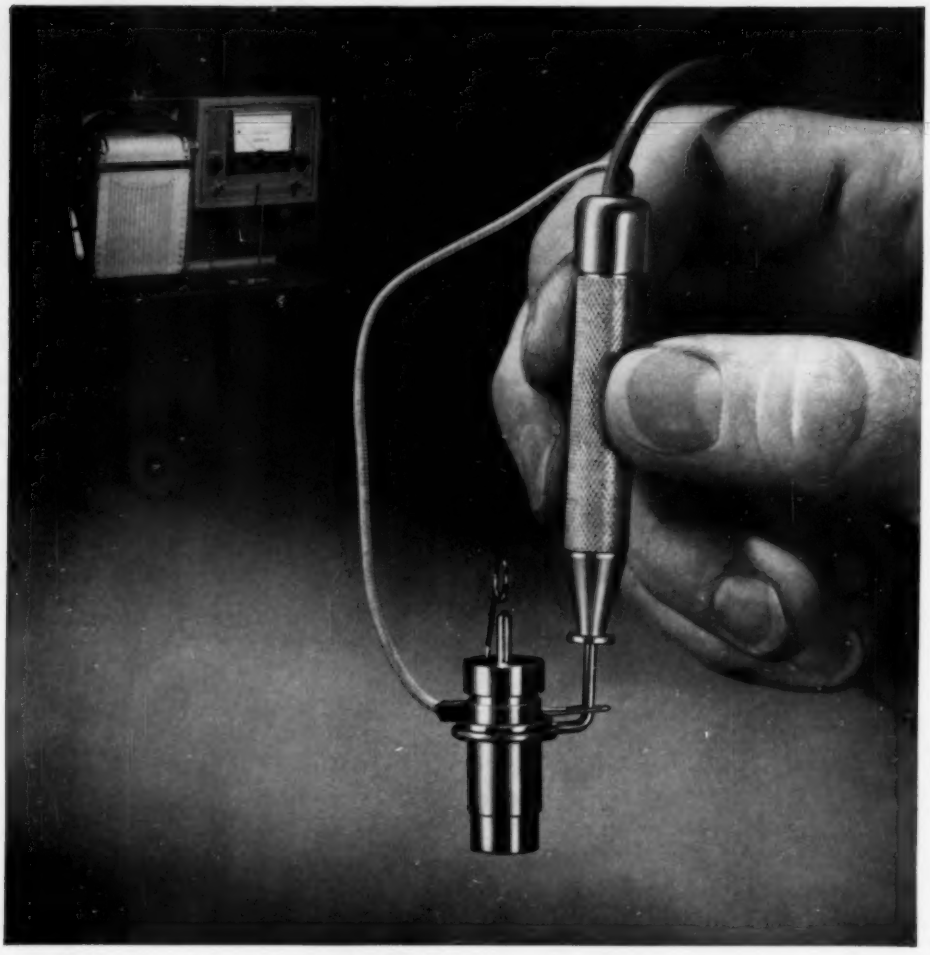

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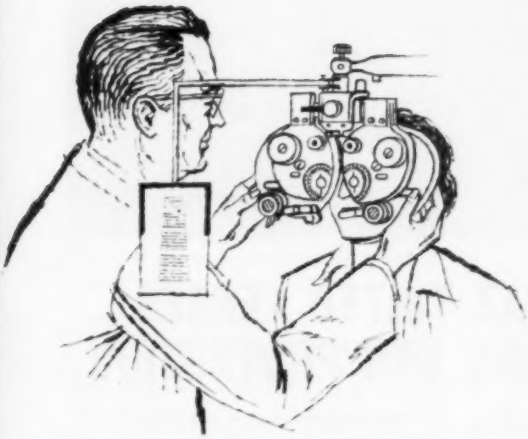
There is an area of preference in all things, and the choice of a multifocal is no exception. Some refractionists prefer the Vision-Ease D-style bifocal, the popular straight-top segment; some prefer a round segment for other reasons. The curved-top segment has found a wide acceptance among professional men because it combines the advantages of the straight-top with the advantages of the round segment.



For practitioners who prefer the curved-top segment, Vision-Ease proudly offers the C-style bifocal, in 20 and 22mm segments. This fine lens offers refractionists a wide range of availabilities in both standard forms from stock and non-standard forms through the famed Vision-Ease Special Order Service. It is carried in all Vision-Ease Branch Stock Offices as a standard item, in Tints and in White.

The Vision-Ease C-style bifocal features a precise, color-free segment and compensated curves for your laboratory's convenience. Whenever the Rx calls for a curved-top bifocal, specify Vision-Ease C-style . . . for the finest in Vision-Ease Quality!

VISION-EASE

THE VISION-EASE CORPORATION
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These fine curved-top bifocals are available as regular stock items in most-wanted base curves, adds and tints. For non-standard availabilities, check your laboratory or the nearest Vision-Ease Stock Office.

VISION-EASE C-20
20mm curved-top

VISION-EASE C-22
22mm curved-top

It is a matter of pride that Vision-Ease Multifocals are available to the professions only through established, ethical suppliers; Vision-Ease does not engage in any form of direct distribution and special work is performed only on request of a recognized Vision-Ease supplier.

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Zeiss UROPAL lenses, with fully corrected curve, are renowned throughout the world for their quality and they are the only lenses, with light tint, that filter out the harmful ultra violet and infra-red rays. The topaz tint is cosmetically becoming to the wearer and gives the impression of lightness and brilliance which is so helpful to the sight even in artificial light without the penalties imposed by invisible rays, which come from all sources of light.

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ZEISS PUNKTAL LENSES . . . classic white lenses that give a point focal image and broad field of vision throughout the lenses, are available in a wide range of powers.

ZEISS UMBRAL LENSES . . . give perfect eye protection, in summer and winter, against excessive glare and infra red and ultra violet rays, yet the even brown tint retains colors in their natural proportions.

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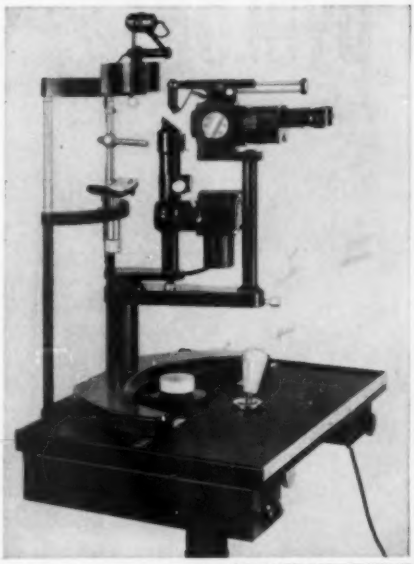

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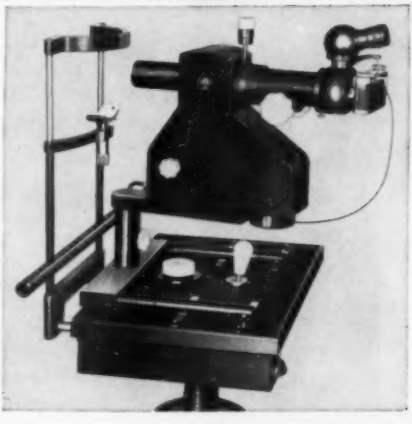

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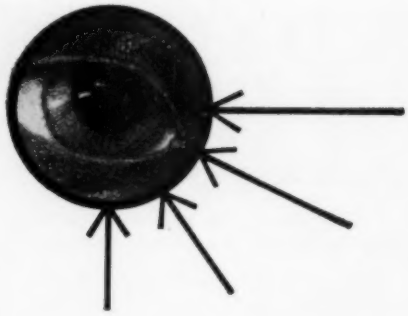

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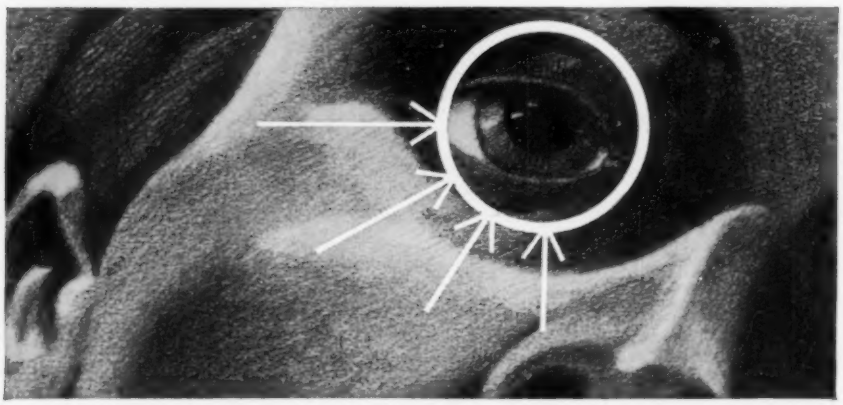
1. Swan, K. C.: Tr. Am. Acad. Opth. *60*:368, 1956.
2. Arora, R. B., et al.: E. E. N. T. Monthly *34*:593, 1955.
3. Florestano, H. J., and Bahler, M. E.: J. Am. Pharm. A. (Scient. Ed.) *45*:360, 1956.



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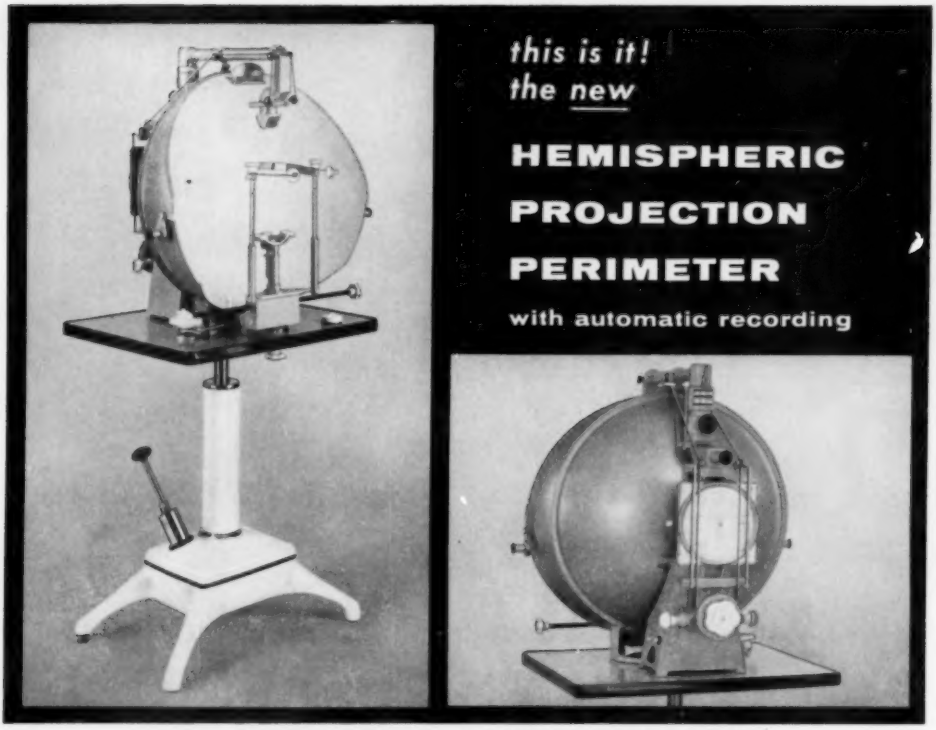

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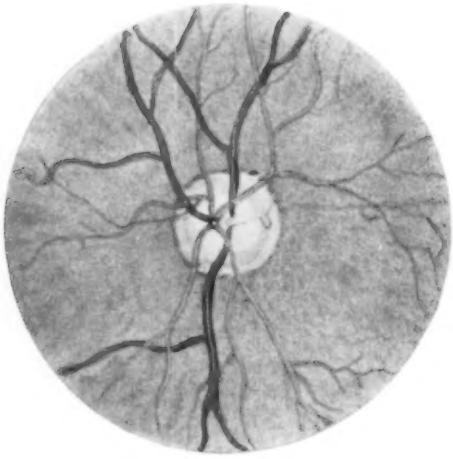

Fig. 1

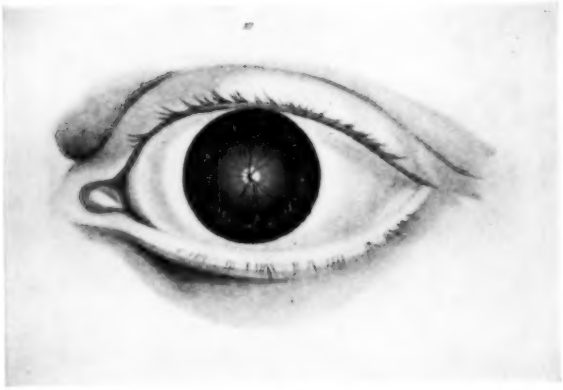

Fig. 2

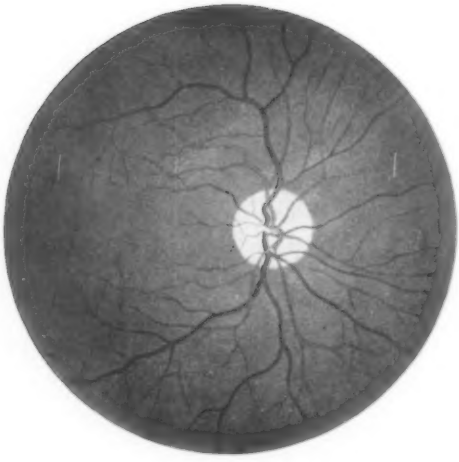

Fig. 3

AMERICAN JOURNAL OF OPHTHALMOLOGY

VOLUME 49 MAY, 1960 NUMBER 5, PART I

THE ATLASES OF OPHTHALMOSCOPY: A BIBLIOGRAPHY, 1850-1960*

THOMAS E. KEYS,† M.A., AND C. WILBUR RUCKER, M.D.
Rochester, Minnesota

In commemoration of the centenary of the invention of the ophthalmoscope, we compiled a comprehensive catalogue of "Atlases of Ophthalmoscopy" for an exhibit of atlases at the meeting of the American Medical Association in 1950. This catalogue was privately printed, and the supply is now exhausted. To make the list available to interested readers, Dr. Vail suggested that we bring it up to date, and he has graciously offered to reprint it in THE JOURNAL.

In compiling our list, we have found it difficult to decide whether some books are atlases or merely illustrated texts, and we have been forced in some cases to make purely arbitrary decisions. We have omitted manuals unless they were abundantly illustrated or were of special significance. Texts on ophthalmology which incidentally contain some pictures of the retina have not been included.

Ophthalmoscopy developed from a simple eye speculum that a young professor, Hermann Helmholtz, constructed with a few glass slides and some cardboard for the purpose of demonstrating to his students a principle in optics. He wished to explain why the pupil of the eye appeared black and how under special circumstances it could be made to appear red. The phenomenon and its explanation were well enough known at that time. But he went a step farther and devised a mirror which not only illuminated the interior of the eye but permitted a view of the retina.

He announced his invention to the Berlin Physical Society on December 6, 1850, in a paper presented by his friend, Du Bois-Reymond.[1] On December 17, 1850, he wrote to his father as follows:[2]

> In regard to time-measurements I have at present no new results, but have devoted myself to the construction of fresh apparatus and necessary preliminaries. But I have made a discovery during my lectures on the Physiology of the Sense-organs, which may be of the utmost importance in ophthalmology. It was so obvious, requiring, moreover, no knowledge beyond the optics I learned at the Gymnasium, that it seems almost ludicrous that I and others should have been so slow as not to see it. It is, namely, a combination of glasses, by means of which it is possible to illuminate the dark background of the eye, through the pupil, without employing any dazzling light, and to obtain a view of all the elements of the retina at once, more exactly than one can see the external parts of the eye without magnification, because the transparent media of the eye act like a lens with a magnifying power of twenty. The blood-vessels are displayed in the neatest way, with the branching arteries and veins, the entrance of the optic nerve into the eye, &c. Till now a whole series of most important eye-diseases, known collectively as black cataract, have been terra incognita, because the changes in the eye were practically unknown, both during life, and, generally speaking, after death. My discovery makes the minute investigation of the internal structures of the eye a possibility. I have announced this very precious egg of Columbus to the Physical Society at Berlin, as my property, and am now having an improved and more convenient instrument constructed to replace my pasteboard affair. I shall examine

* From the Mayo Clinic, and the Mayo Foundation, Graduate School, University of Minnesota.

† Librarian, Mayo Clinic; assistant professor of history of medicine, Mayo Foundation, Graduate School, University of Minnesota.

Fig. 1 (Keys and Rucker). The first published illustration of the fundus of the eye. Taken from Van Trigt, 1853. (Reproduced by courtesy of the National Library of Medicine.)
Fig. 2 (Keys and Rucker). The eye as viewed by indirect ophthalmoscopy. Taken from Ruete, 1854.
Fig. 3 (Keys and Rucker). The background of the normal eye. Taken from Jaeger, 1855.

as many patients as possible with the chief oculist here, and then publish the matter.

The following October saw the publication of his classic *Beschreibung eines Augen-Spiegels. . . .*[3]

Since then more than a hundred atlases dealing with ophthalmoscopy have been printed, many of them beautifully illustrated. The first published illustrations of the fundus of the eye (fig. 1) appeared in the thesis written in Latin for his doctorate by a medical student in Holland in 1853. The writer, A. C. Van Trigt (see list of "Atlases arranged alphabetically with annotations"), had selected for his subject the eye speculum recently invented by Professor Helmholtz of Königsberg. Ruete invented the indirect method of ophthalmoscopy in 1852 and, in 1854, published a monograph including a number of pictures of the fundus (see list of atlases). With his method the examiner sees not only the fundus filling the pupillary area, but also the iris, sclera and even the lids. Ruete drew all he saw, as in Figure 2. Jaeger of Vienna published a collection of paintings of the fundus of the eye in 1855 (see list of atlases) and published enlarged volumes in 1869 and 1870. He took infinite pains with his illustrations and stated in the introduction to one of his books that some paintings required 20 to 40 sittings of two to three hours each (for example, fig. 3). In most of the early texts on ophthalmoscopy and in some of the later ones the illustrations were painted by the ophthalmologists themselves.

References

1. Helmholtz, H.: Ueber das Leuchten der Augen (Dec. 6, 1850). Fortschritte der Physik in den Jahren 1850 und 1851. Dargestellt von der physikalischen Gesellschaft zu Berlin. Berlin, Georg Reimer, 1855, VI and VII Jahrgang. Nachrichten, VII.

2. Koenigsberger, L.: Hermann von Helmholtz. (Translated by Frances A. Welby.) Oxford, Clarendon Press, 1906, pp. 73-74.

3. Helmholtz, H.: Beschreibung eines Augen-Spiegels zur Untersuchung der Netzhaut im lebenden Auge. Berlin, A. Förstner'sche Verlagsbuchhandlung, 1851, 43 pp., 1 l., 1 pl. (Translation by Hollenhorst, R. W.: Description of an ophthalmoscope for examining the retina in the living eye. A.M.A. Arch. Ophth., **46**:565-583 [Nov.] 1951.)

The atlases arranged alphabetically with annotations

Adam, Curt: Ophthalmoskopische Diagnostik an der Hand typischer Augenhintergrundsbilder. Mit besonder Berücksichtigung der für die Allgemein-Medizin wichtigen Fälle für Arzte und Studierende . . . Mit 86 mehrfarbigen Abbildungen auf 48 Tafeln und 18 Textabbildungen. Berlin und Wien, Urban und Schwarzenberg, 1912. xxi, 232 pp. 48 col. pl.

Note: These are excellent colored reproductions of paintings by the author who worked at the University Eye Clinic in Berlin. They represent the inverted image of indirect ophthalmoscopy magnified 10 times. This was a popular text during the First World War and for a decade or more after it ended.

———: Diagnostic ophtalmoscopique d'après des reproductions types de fonds d'yeux. Avec examen spécial des cas importants de médecine générale à l'usage des médecins et des étudiants . . . Trad. par F. Bourdier . . . avec une préface par (F.) de Lapersonne . . . Paris, Librarie le françois (1913). xxi, 242 pp., 48 col. pl.

———: Ophthalmoscopic Diagnosis based on Typical Pictures of the Fundus of the Eye with Special Reference to the Needs of General Practitioners and Students . . . Translated by Matthias Lanckton Foster . . . with 86 colored pictures on 48 plates and 18 illustrations in the text. New York City, The Medical Art Agency, Rebman Co., sole agents, ©1913. xx, 229 pp., illus., 48 col. pl.

Atkinson, Donald Taylor, 1874- : The Ocular Fundus in Diagnosis and Treatment . . . Philadelphia, Lea and Febiger (©1937). 142 pp., illus., 58 col. pl.

Note: The plates, both colored and black and white, are wholly the work of the author himself, not that of a professional artist.

BADER, CHARLES, 1825-1899: The Natural and Morbid Changes of the Human Eye, and Their Treatment. With an atlas of 10 plates. London, N. Trübner & Co., 1868. viii, 505 pp. Accompanied by "Plates illustrating the natural and morbid changes of the human eye . . ." 32 pp. and 10 plates, 5 of the fundus in col.

Note: The fundus illustrations are poor reproductions from the originals painted by Mr. R. Schweizer of Clerkenwell. Jaeger in his *Ophthalmoskopischer Hand-Atlas* (1869) referred to them contemptuously.

BARKER, W. B.: *see* Haab, O.

BAYER, JOSEPH, 1847-1925: Bildliche Darstellung des gesunden und kranken Auges unserer Hausthiere . . . Wien, W. Braumuller, 1891-1892. I und II Abth., 13 l., 12 col. pl.; 13 l., 13 col. pl.

Note: Diseases of the eye of the horse are emphasized in this early veterinary ophthalmoscopy.

BEARD, CHARLES HEADY, 1855-1916: . . . Ophthalmic Semiology and Diagnosis. Philadelphia, P. Blakiston's Son and Co., 1913. xi, 400 pp., 13 col. pl. (This volume is one of a series entitled: "An International System of Ophthalmic Practice," edited by Walter L. Pyle.)

Note: Disorders of the optic nerve head and retina are discussed in their relationship to general diseases. The original drawings of the fundi were painted in color by the author, but were reproduced in black and white in order to minimize the expense of publication.

BEDELL, ARTHUR JOSEPH, 1879- : Photographs of the Fundus Oculi; a Photographic Study of Normal and Pathological Changes Seen with the Ophthalmoscope . . . An atlas containing 95 plates, 324 single pictures and 272 stereoscopic photographs. Philadelphia, F. A. Davis Co., 1929. 317 pp., 95 pl. (Also issued in 2 v.)

Note: This is the second atlas of photographs to be published and was preceded only by that of Dimmer and Pillat; it is the first to be printed in English. Many of the illustrations are stereophotographs.

BENNETT, R. W.: *see* Bothman, L.

BERARD, E.: *see* Jaeger, E.

BONACCOLOTO, G.: *see* Marzio, Q. di

BONAMOUR, GEORGES, 1907- : Étude clinique du fond d'oeil dans l'hypertension artérielle. Lyon (Privately printed, 1936). 5 p. l., 141 pp., 8 l., illus. (Travail de la clinique ophtalmologique du Professeur Bonnet. Préface par A. Dumas.)

BONNET, P.: *see* Bonamour, G.

BONNET, PAUL, 1884- : . . . Altérations de la rétine en rapport avec les affectiones générales. Atlas ophtalmoscopique II. Rapport présentè à la Société française d'ophtalmologie le 18 Mai 1947 . . . Paris, Masson et Cie, 1945. xii, 253 pp., 1 l., (tables des matières) illus., 36 col. pl.

Note: This monograph deals chiefly with changes in the retina produced by blood dyscrasias and by diabetes mellitus. The colored illustrations are superior to those of the earlier French atlases.

BOTHMAN, LOUIS, 1893-1949, and BENNETT, REUEL W.: Fundus Atlas; Stereoscopic Photographs of the Fundus Oculi. Chicago, Year Book Publishers, 1939. 3 l., 50 numbered cards, illus.

Note: This is a collection of black-and-white stereograms made with the aid of the reflex-free Nordenson fundus camera and enlarged about three times. Each is accompanied by a brief case report and a description of the fundus picture.

BOUCHUT, J. EUGÈNE, 1818-1891: Du diagnostic des maladies du système nerveux par l'ophthalmoscopie . . . Paris, Germer Baillière, 1866. xx, 503 pp.; illus., 24 col. pl.

Note: The atlas is composed of 24 chromolithographs prepared by the author, which were printed separately and pasted on the appropriate pages. They are inferior to the German plates of the same period.

———: Atlas d'ophtalmoscopie médicale et de cérébroscopie, montrant chez l'homme et chez les animaux les lésions du nerf optique, de la rétine et de la choroïde produites par les maladies du cerveau, par les maladies de la moelle épinière et par les maladies constitutionnelles et humorales. Paris, J.-B. Baillière et Fils, 1876. viii, 148 pp., 14 pl.

Note: This is an early example of ophthalmoscopy as a guide to general diagnosis. It is reviewed as inaccurate and careless throughout in *Jahresber. ü. d. Ophth.*, **7**:375-382, 1876.

BOURDIER, F.: *see* Adam, C.

CATTANEO, DONATO: . . . Oftalmoangioscopia . . . Bologna, L. Cappelli, 1947. 636 pp., illus., 71 col. pl.

Note: Each plate consists of a photograph of the fundus in black and white and beneath it a painting of the same fundus in color, which brings out details not always distinct in the photograph. The importance of impaired circulation in the retina is emphasized.

CLARKE, ERNEST, 1857-1932: . . . The Fundus of the Human Eye, an Illustrated Atlas for the Physician . . . Oxford University Press; London, Humphrey Milford, 1931. 8 p. l., 51 col. pl.

Note: Fifty-one colored paintings selected from the collection of Messrs. Theodore Hamblin of London, opticians, are reproduced with brief descriptive legends.

CLARKE, E.: *see* Haab, O.

CLERICI, ANTONIO: Retinografia; studio fotographico del fondo oculare. Milano, Istituto Editoriale Cisalpino, 1943. 269 pp., 130 photographs in black and white and 8 in color.

Note: A collection of fundus photographs, most of them enlarged to about 17 cm. in diameter. Accompanying each photograph is a short description including a brief account of the patient and a paragraph of discussion.

———: Studio documentato del fondo oculare: alterazioni circolatorie, 133 retinografie. Milano, A. Fattorini, 1957. 209 pp., 2 ll., 133 pl.

Note: The originally excellent photographs have lost detail in reproduction by off-set lithography.

COUADAU, A.: *see* Tillé, H.

CUÉNOD, A.: *see* Haab, O.

DANIS, MARCEL, 1883-1943: . . . Les aspects normaux et les anomalies congénitales du fond de l'oeil. Atlas ophtalmoscopique. Rapport présenté à la Société d'ophtalmologie le 25 Mai 1940 . . . Paris, Masson et Cie, 2 p. l., 276 pp., illus., 38 col. pl.

Note: This is a consideration of the anatomic basis of congenital anomalies. The colored plates of the fundi are from paintings by the author.

DELGADO JUGO, F.: *see* Liebreich, R. L.

DIMMER, FRIEDRICH, 1855-1926: Der Augenspiegel und die ophthalmoskopische Diagnostik . . . Leipzig und Wien, Toeplitz und Deuticke, 1887. vii, 175 pp., 73 illus.

———: Der Augenspiegel und die ophthalmoskopische Diagnostik. 2 umgearbeitete und vermehrte Aufl. Leipzig und Wien, F. Deuticke, 1893. ix, 206 pp., 91 illus.

———: Die Photographie des Augenhintergrundes. Wiesbaden, J. F. Bergmann, 1907. ix, (1 l.), 742 pp., 15 pl.

Note: This is a text on fundus photography with an exposition of the basic principles, a description of the author's apparatus and an explanation of its use. It contains 12 plates of fundus photographs.

———: Der Augenspiegel und die ophthalmoskopische Diagnostik . . . Dritte Aufl. Leipzig und Wien, Franz Deuticke, 1921, xi, 1 p., 633 pp., 11 pp., illus., 16 pl.

Note: This is a comprehensive text with 10 pages of fundus photographs at the end.

———: Atlas photographischer Bilder des menschlichen Augenhintergrundes . . . von Friedrich Dimmer und Arnold Pillat . . . Leipzig und Wien, Franz Deuticke, 1927. 30 pp., 84 pl.

Note: Throughout his life Dimmer had planned to publish an atlas of photographs of the fundus, but died before the project was completed. The task was concluded by one of his students, Dr. Pillat.

DUMAS, A.: *See* Bonamour, G.

ELWYN, HERMAN, 1885- : Diseases of the Retina . . . Philadelphia and Toronto, the Blakiston Company, 1946. xi, 587 pp., illus., 19 col. pl.

———: Diseases of the Retina. Ed. 2 . . . New York, Blakiston [1953]. 713 pp., 243 illus.

Note: This is an admirable text. The emphasis here is on the ocular manifestations of disease. It is complete enough for the graduate student, but is not burdened with unnecessary detail.

ERBAUGH, JOHN K.: Principles of Ophthalmoscopy. Springfield, Illinois, Charles C Thomas, 1958. x, 69 pp., 8 col. pl.

FISHER, WILLIAM ALBERT, 1859-1944: Ophthalmoscopy, Retinoscopy and Refraction . . . Chicago (Privately printed for the author, 1922). 5 p. l., 218 pp., 3 l., illus., 24 col. pl. A duplicate set of col. pl. inserted at the end of the volume.

———: Ophthalmoscopy, Retinoscopy and Refraction. Ed. 2. Philadelphia, F. A. Davis Co., 1927. 291 pp., illus., 24 col. pl. A duplicate set of col. pl. inserted at the end of the volume.

———: Ophthalmoscopy, Retinoscopy and Refraction. Ed. 3. Philadelphia, F. A. Davis Co., 1931. 291 pp., pl.

FOSTER, M. L.: *see* Adam, C.

FROMAGET, C.: *see* Nicolas, E.

FROST, WILLIAM ADAMS, 1853-1935: The Fundus Oculi with an Ophthalmoscopic Atlas, Illustrating Its Physiological and Pathological Conditions . . . Edinburgh and London, Young J. Pentland, 1896. New York, the Macmillan Company. xviii, 1 p. l., 228 pp., 107 figs. on 47 col. pl. with legends and explanatory matter between.

Note: The illustrations were painted by A. W. Head and reproduced by color lithography. They were the finest plates of the fundus produced before the time of the electric ophthalmoscope. It was a deservedly popular text in its day.

FUCHS, ADALBERT, 1887- : Die Erkrankungen des Augenhintergrundes . . . Wien, Franz Deuticke, 1943. xv, 287 pp., 44 col. pl.

———: Diseases of the Fundus Oculi with Atlas. Translated by Erich Pressburger, edited by Abraham Schlossman. 1st English ed. Philadelphia, the Blakiston Company, 1949. xiv, 337 pp., illus., 44 col. pl.

Note: This is an amplified English translation of a text published 6 years previously in German. It attempts to correlate the ophthalmoscopic picture with basic pathology.

GALEZOWSKI, XAVIER, 1832-1907: Traité iconographique d'ophthalmoscopie, comprenant la description des différents ophthalmoscopes, l'exploration des membranes internes de l'oeil et le diagnostic des affections cérébrales et constitutionnelles . . . Paris, J.-B. Baillière et Fils, 1876. viii, 286 pp., 20 col. pl.

Note: The author was born in Poland, studied medicine in St. Petersburg and practiced and taught in Paris. His chief interest was the relation of the eye to diseases of the brain.

———: Traîté iconographique d'ophthalmoscopie, comprenant la description des différents ophthalmoscopes, l'exploration des membranes internes de l'oeil et la diagnostic des affections cérébrales et constitutionnelles . . . 2 éd. . . . Paris, J.-B. Baillière et Fils, 1886. vi, 355 pp., illus., 28 col. pl.

Note: This was one of the more widely used atlases of the time. The illustrations are reproductions from paintings by the author.

GOWERS, WILLIAM RICHARD, 1845-1915: A Manual and Atlas of Medical Ophthalmoscopy. London, J. and A. Churchill, 1879. xi, 352 pp., 16 pl.

Note: The author was a famed London neurologist. The illustrations in his text were reproduc-

tions of his own paintings, a few in natural color, the others in sepia. He felt sepia represented pathologic conditions more exactly.

———: A Manual and Atlas of Medical Ophthalmoscopy. Ed. 2. London, J. and A. Churchill, and Philadelphia, P. Blakiston, 1882. xvi, 384 pp., 16 pl.

———: A Manual and Atlas of Medical Ophthalmoscopy . . . Ed. 3, rev. . . . Ed. with the assistance of Marcus Gunn . . . London, J. and A. Churchill, and Philadelphia, P. Blakiston's Son & Co., 1890. xi, 330 pp., illus., 12 pl.

———: A Manual and Atlas of Medical Ophthalmoscopy . . . Ed. 4. Ed. by the author and Marcus Gunn . . . London, J. and A. Churchill, 1904, xi, 318 pp., illus., 10 pl.

———: Die Ophthalmoskopie in der inneren Medizin. Ein Handbuch und Atlas . . . Nach der 3. englischen Aufl. ubersetzt von Karl Grube. Leipzig und Wien, Franz Deuticke, 1893. iv, 353 pp., 12 pl.

GRUBE, K., *see* Gowers, W. R.

GUÉRINEAU, JOSEPH-DÉSIRÉ: Du diagnostic différentiel à l'aide de l'ophthalmoscope des amauroses vraie et simulée devant les conseils de révision. Paris, P. Asselin, 1860. 2 p.l., 104 pp., 21 col. pl., III.

Note: This elementary manual was published as an aid to surgeons in evaluating alleged blindness on the part of recruits inducted into military service. The author's colored illustrations are lacking in adequate detail.

GUIST, GUSTAV: Coincident Ophthalmoscopy and Histology of the Optic Nerve . . . Vienna, Published by the author, 1934. 2 v. illus., v. 1, text, v. 2, atlas.

Note: This work is unique in that the illustrations and accompanying microscopic sections were obtained from the same eyes.

GUNN, M., *see* Gowers, W. R. 1890 and 1904.

HAAB, OTTO, 1850-1931: Atlas und Grundriss der Ophthalmoskopie und ophthalmoskopischen Diagnostik. München, J. F. Lehmann, 1895. vi, 69 pp., 64 pl., 32 l. (Lehmann's Medicin. Handatlanten, Band 7.)

Note: This was a popular atlas designed especially for students. It appears in 5 German, 3 French and 5 English editions. Haab practiced and taught at the Eye Clinic in Zurich, Switzerland. The illustrations in the atlas were drawn by a professional artist under Haab's supervision.

———: . . . Atlas und Grundriss der Ophthalmoskcopie und ophthalmoskopischen Diagnostik. Mit 138 farbigen und 7 schwarzen Abbildungen . . . 2 Aufl. München, J. F. Lehmann, 1897. ix (1 p.) 81 pp., 40 l., 79 pl., 1 tab. (Lehmann's Medicin. Handatlanten, Band 7.)

———: . . . Atlas und Grundriss der Ophthalmoskopie und ophthalmoskopischen Diagnostik . . . 3 Aufl. München, J. F. Lehmann, 1900. ix, 82 pp., 48 l., 82 pl. (Lehmann's Medicin. Handatlanten, Band 7.)

———: . . . Atlas und Grundriss der Ophthalmoskopie und ophthalmoskopischen Diagnostik . . . 4 Aufl. München, J. F. Lehmann, 1904. xi, 83 pl., 82 pp. (Lehmann's Medizin. Handatlanten, Band 7.)

———: . . . Atlas und Grundriss der Ophthalmoskopie und ophthalmoskopischen Diagnostik . . . 5 Aufl. München, J. F. Lehmann, 1908. xiii, 88 pp., 87 pl. (Lehmann's Medizin. Handatlanten, Band 7.)

———: Atlas manuel d'ophtalmoscopie. Éd. française par Albert Terson (et) A. Cuénod. Paris, J. B. Baillière et Fils, 1896. x, 244 pp., 64 pl.

———: Atlas manuel d'ophtalmoscopie. Éd. fraiçaise par . . . Albert Terson (et) A. Cuénod. 2 éd., très augmentée. Paris, J. B. Baillière et Fils, 1900. 276 pp., 80 pl.

———: Atlas manuel d'opthalmoscopie. Éd. française par . . . Albert Terson (et) A. Cuénod. 3 éd., très augmentée . . . Paris, J. B. Baillière et Fils, 1901. 276 pp., 80 pl.

———: An Atlas of Ophthalmoscopy . . . With an Introduction to the Use of the Ophthalmoscope . . . Tr. and ed. by Ernest Clarke . . . London, Baillière, Tindall and Cox, and New York, William Wood and Co., ©1895. 55 pp., 64 col. pl.

———: An Atlas of Ophthalmoscopy with an Introduction to the Use of the Ophthalmoscope. Translated and edited by Ernest Clarke. London, Baillière, Tindall & Cox, 1898.

Note: The title page differs from 1895 edition, but contents are similar.

———: An Atlas of Ophthalmoscopy . . . Tr. and ed. by W. B. Barker . . . London, British Optical Association, 1928. 1 pl., 230 pp., 87 (i.e. 88) mounted col. pl., diags.

———: Atlas and Epitome of Ophthalmoscopy and Ophthalmoscopic Diagnosis . . . Authorized translation from the 3 rev. and enl. German ed. Ed. by G. E. de Schweinitz . . . with 152 colored lithographic illustrations. Philadelphia and London, W. B. Saunders Co., 1901. 85 pp., illus., 89 col. pl.

———: Atlas and Epitome of Ophthalmoscopy and Ophthalmoscopic Diagnosis. Ed. by G. E. de Schweinitz. 2 Am. ed. from 5 Ger. ed. Philadelphia and London, W. B. Saunders Co., 1909. 94 pp., 152 pl.

———: Skizzenbuch zur Einzeichnung ophthalmoscopischer Beobachtungen des Augen-Hintergrundes . . . 2 Ausg. München, J. F. Lehmann, 1895. 8 pp., col. pl.

Note: Haab made a "sketch book" available for students of ophthalmoscopy. It provided colored plates, some showing typical normal fundi. The student was to trace any observed deviations on these plates and to attempt to arrive at a diagnosis by comparing his findings with those in Haab's atlas.

———: Skizzenbuch zur Einzeichnung von Augenspiegel-Gildern. 2 verb. Aufl. München, J. F. Lehmann, 1898. 14 l., 30 pl.

HEAD, A. W.: *see* Frost, W. A.; Johnson, G. L.; Wood, C. A.

Note: A. W. Head made the illustrations for the atlases of these ophthalmologists.

HULKE, JOHN WHITAKER, 1830-1895: A Practical Treatise on the Use of the Ophthalmoscope, being the Essay for Which the Jacksonian Prize in the Year 1859 Was Awarded by the Royal College of Surgeons of England . . . London, John Churchill, 1861. viii, 70 pp., illus., ix-x, 4 col. pl.

Note: A few of the colored plates are original; a few are copied after Jaeger.

ILYINSKI, A. I.: Ophtalmoskopicheskii atlas, soderjat shii Kratkuju Hoiju ophtalmoskopa i xviii raskrashennich chromolitographicheskich. Moskva, V. J. Barbry, 1887. 24 pp., 3 col. pl.

Note: This Russian atlas contains a short history of the ophthalmoscope and 18 chromolithographs of the fundi. Only one copy can be traced in this country, that in the National Library of Medicine.

INOUYE, T. [Talsuchichiro]: Inouye Kanrio shio [Inouye's Ophthalmoscopic Atlas]. (Tokio, S. Takahasi, 1893.) v. 1, 5 col. pl. fol.

Note: This is superior to Yamada's atlas (1881). The illustrations are handsomely done and are reproductions of colored paintings. Only one copy has been traced in the United States, that in the National Library of Medicine.

ISHIHARA, SHINOBU: Atlas of the Fundus Oculi. Ed. 3. Nippon Isho Shupan Kabushiki Kaisha (Japanese Medical Publications Corporation [or Company?]), Tokyo, Kyoto, 1948. 225 col. illus.

Note: First edition was published in 1935, second edition in 1942, according to a note in this third edition. The first two were not available for examination. The illustrations appear inverted as they were drawn with indirect ophthalmoscopy. They have a browner cast than Europeans are accustomed to seeing in their atlases. The entire text is in Japanese. A diagnosis for each illustration is added in Latin.

———: Atlas of the Fundus Oculi. Ed. 4. Nippon Isho Shupan Kabushiki Kaisha (Japanese Medical Publications Corporation [or Company?]), Tokyo, Kyoto, 1952. 302 pp., 225 col. illus.

Note: In this edition the Japanese characters have been changed to a simpler form than were employed in previous editions. The illustrations and text remain the same.

JAEGER, EDUARD, RITTER VON JAXTTHAL, 1818-1884: Ueber Staar und Staaroperationen nebst anderen Beobachtungen und Erfahrungen . . . Wien, L. W. Seidel, 1854. viii, 128 pp., 32 l., 10 pl.

Note: This is not an atlas, but is included since it contains early black-and-white reproductions of the fundus from drawings by Jaeger.

———: Beiträge zur Pathologie des Auges . . . mit Abbildungen im Farbendruck . . . Wien, Kaiserlich Königlichen Hof und Staatsdruckerei, 1855. 56 pp., 21 col. pl. fol.

Note: The 21 colored illustrations were painted by Jaeger. The textual material consists of case reports and descriptions of the plates.

———: Beiträge zur Pathologie des Auges. 2 Aufl. Wien, Kaiserlich Königlichen Hof und Staatsdruckerei, 1870. 2 p.l., 223 pp., 73 col. pl. fol.

Note: The second edition is enlarged to include magnificent reproductions of 73 colored fundus paintings by the author. Each plate is on a separate page. The accompanying text presents a case report as well as a complete description of each plate.

———: Ergebnisse der Untersuchung des menschlichen Auges mit dem Augenspiegel (mit viii Tafeln). Sitzungsb. d. k. Akad. d. Wissensch. Math.-naturw. Cl., Wien, 15: 319-344, 1855. Also published as reprint. Wien, Kaiserlich Königlichen Hof und Staatsdruckerei, 1855. 28 pp., 8 col. pl.

Note: This is scarcely an atlas, for it is a reprint of an article from a periodical. It is included as an early example of colored illustrations of the fundus.

———: Ophthalmoskopischer Hand-atlas . . . Wien, Kaiserlich Königlichen Hof und Staatsdruckerei, 1869. xviii, 236 pp., 29 col. pl. (128 figs.)

Note: The author prepared his atlas with exceeding care. He made his own paintings, from which the colored plates were reproduced. Jaeger required, in most cases, from 20 to 50 sittings of from 2 to 3 hours each to make the sketch of one image alone.

———: Ophthalmoskopischer Hand-atlas. Neu bearbeitet und vergrössert von Maximilian Salzmann. Leipzig und Wien, Franz Deuticke, 1890. xi, 88 pp., 31 pl.

———: Ophthalmoskopischer Hand-atlas. Neu bearbeitet und vergrössert von Maximilian Salzmann . . . 2 Aufl. . . . Leipzig und Wien, Franz Deuticke, 1894. xv. 92 pp., 32 col. pl. with 140 figs.

———: Atlas d'ophthalmoscopie, remanié et augmenté par Maximilian Salzmann. Traduction française du docteur Eduard Berard. Paris, Asselin et Houzeau, 1890. xii, 94 pp., 31 col. pl.

———: Ophthalmoscopical Atlas. Rev. and enl. by Maximilian Salzmann. English tr. by William A. Martin . . . Leipzig, Franz Deuticke; London, Williams and Norgate; New York, B. Westermann and Co., 1890, xii, 86 pp., 31 col. pl.

———: *see* Wecker, L. de

JEAN, GEORGE WILLIAM: Ophthalmoscopic Diagnosis for General Practitioners and Students . . . London and New York, E. B. Meyrowitz, 1915. vii, 123 pp., 68 illus.

Note: This is a small text. The illustrations are black-and-white copies of colored pictures previously published by others.

JENNINGS, J. E.: A Manual of Ophthalmoscopy for Students and General Practitioners. Philadelphia, P. Blakiston's Son & Co., 1902. 180 pp., 95 illus. and col. front.

JOHNSON, GEORGE LINDSAY, 1853-1943: Contributions to the Comparative Anatomy of the Mammalian Eye, chiefly based on Ophthalmoscopic Examination. Royal Soc. of London, Phil. Tr. Ser. B. 194:1-82, 30 pl., 26 in col., 1901.

Note: Johnson demonstrated that the background of the eye could be a useful guide to classification of mammals. The illustrations are reproductions of paintings of the ocular fundi by A. W. Head. An entertaining account of Head's experiences painting the fundi of the animals appears in "Eye to Eye with Wild Beasts" by Turner Morton in Pearson's Magazine, London, **14**:378-389 (July-Dec.) 1902.

———: A Pocket Atlas and Text-book of the Fundus Oculi, with Note and Drawing Book . . . with Drawings from Life by Arthur W. Head . . . London, Adlard and Son, Bartholomew Press, 1911. viii, 1 l., 205 pp., illus., 27 col. pl. and front.

Note: This is an excellent small volume for students and is illustrated by A. W. Head. A drawing book is tied to the back cover. In it the relative positions of the disk and macula are indicated in diagrams, enabling the student quickly to pencil in any pathologic detail.

KNAPP, A. H.: *see* Oeller, J. N.

KÖLLNER, HANS: Der Augenhintergrund bei Allgemeinerkrankungen, ein Leitfaden für Arzte und Studierende . . . Berlin, Julius Springer, 1920. vi, 185 pp., illus.

Note: This text for students, with most of its illustrations in color, demonstrates the eye findings in general medical diseases.

LAGRANGE, FELIX, 1857-1928: Atlas d'ophtalmoscopie de guerre . . . Texte français et anglais . . . Paris, Masson et Cie, 1918. lv, 205 unnumbered leaves. 100 illus., 20 in col. The English text by Dr. Menier (de Decazeville).

Note: Various types of injury to the eye occurring as a result of trauma are pictured and explained. The text runs concomitantly in French and English.

LAPERSONNE, F. DE: *see* Adam, C.

LIEBREICH, RICHARD L., 1830-1917: Atlas der Ophthalmoscopie. Darstellung des Augengrundes im gesunden und krankhaften Zustande . . . Berlin, August Hirschwald; Paris, Germer Baillière, 1863. x, 42 pp., fol., 12 col. pl. Text in German and French. (French title page as follows: Atlas d'ophthalmoscopie représentant l'état normal et les modifications pathologiques du fond de l'oeil visibles à l'ophtalmoscope, etc.)

Note: The author was an assistant to Helmholtz at Königsberg at the time of the invention of the ophthalmoscope, and learned to use the instrument from the inventor himself. Later he taught and practiced in Paris. The illustrations are reproductions of the author's own paintings.

———: Atlas der Ophthalmoscopie. Darstellung des Augengrundes im gesunden und krankhaften Zustande. Enthaltend 12 Tafeln mit 59 Figuren in Farbendruck . . . Zweite vermehrte und verbesserte Auflage. Berlin. August Hirschwald, 1870. viii, 31 pp., 12 col. pl.

———: Atlas der Ophthalmoscopie. Darstellung des Augengrundes im gesunden und krankhaften Zustande . . . 3 Aufl. Berlin, August Hirschwald, 1885. 1 p. l., viii, 31 pp., 12 col. pl., 1 folding.

———: Atlas de oftalmoscopia representado el estado normal y las modificaciónes patológicas del fondo del ojo visibles con el oftalmoscopio. Compuesto de 12 láminas que contienen 59 figuras . . . Segunda ed. . . . Trad. al español y adicionado con una introducción sobre el oftalmoscopio . . . por el Dr. Fransisco Delgado Jugo . . . Madrid, Bailly-Baillière; Paris, J. B. Baillière é Hijo; Lourdes, H. Baillière; Nueva-York, Baillière Hermanos [1870]. viii, 12 col. pl., 1 folding.

———: Atlas d'ophthalmoscopie représentant l'état normal et les modifications pathologiques du fond de l'oeil visibles à l'ophthalmoscope. Composé de 12 planches contenant 59 figures tirées en chromolithographie. Accompagnées d'un texte explicatif et dessinées d'après nature . . . 2 éd. augm. Paris, Germer Baillière; Berlin, August Hirschwald, 1870. 2 p. l., iv, 36 pp., 12 col. pl. 1 folding.

Note: The first edition in French was combined with the German, 1863. Here the text is entirely in French.

———: Atlas d'ophthalmoscopie représentant l'état normal et les modifications pathologiques du fond de l'oeil visibles à l'ophthalmoscope. Composé de 12 planches contenant 59

figures tirées en chromolithographie. Accompagnées d'un texte explicatif et dessinées d'après nature . . . 3 éd. augm. Paris, Germer Baillière et Cie, 1885. x, 37 pp., 12 col. pl., 1 folding.

———: Atlas of Ophthalmoscopy Representing the Normal and Pathological Conditions of the Fundus Oculi as Seen with the Ophthalmoscope . . . The text translated by H. Rosborough Swanzy; 2 ed. London, John Churchill and Sons; Berlin, August Hirschwald; Paris, Germer Baillière, 1870. viii, 31 pp., 12 col. pl., 1 folding.

Note: This is the first translation of this work into English.

———: Atlas of Ophthalmoscopy, Representing the Normal and Pathological Conditions of the Fundus Oculi as Seen with the Ophthalmoscope . . . The text translated by H. Rosborough Swanzy. 3 ed. London, J. and A. Churchill, 1885. viii, 31 pp., 12 col. pl., 1 folding.

LONGCOPE, W. T.: *see* Wilmer, W. H.

LORING, EDWARD GREELY, 1837-1888: Textbook of Ophthalmoscopy . . . New York, D. Appleton and Co., 1886-1891. 2 v., illus., 10 pl. in col.

Note: Many of the illustrations are reproductions of drawings by the author. He was the inventor of an ophthalmoscope which was widely used in America and in England for many years.

MAGNUS, HUGO FRIEDERICUS, 1842-1907: Ophthalmoscopischer Atlas . . . Die physiologischen und pathologischen Formen des Augenhintergrundes. Für praktische Aerzte und Studierende, nach der Natur dargestellt . . . Leipzig, W. Engelmann, 1872. 2 p.l., 14 col. pl.

Note: The atlas contains colored lithographs from paintings of the fundus by Magnus and were made while he was assistant to Foerster in the eye clinic at Breslau. No text is included. Magnus also supplied 20 colored paintings of the fundus to John R. Wolfe of Glasgow and they were reproduced in 10 plates in the following work: Wolfe, J. R.: *On Diseases and Injuries of the Eye.* London, J. and A. Churchill, 1882. xii, 10 pl., 452 pp., illus.

MARCHESANI, OSWALD, 1900- and Sautter, Hans: Atlas des Augenhintergrundes. München and Berlin, Urban & Schwarzenberg, 1956-1957. 2 v. 322 pp., 1 l. Erster Band, 1956, "Mit 143 farbigen und 6 schwarzen abbildungen auf 87 Tafeln." Zweiter Band, 1957, "Mit 119 farbigen und 7 schwarzen abbildungen auf 74 Tafeln."

Note: A beautiful atlas; superb illustrations, splendidly reproduced on high-grade glazed paper.

———: Atlas of the Ocular Fundus; Atlas du fond de l'oeil; Atlas del fondo de ojo . . . Tr. by A. Philipp . . . New York, Hafner Publishing Company, Inc., 1959. xii, 161 pl., 262 col. and 13 black-and-white illus.

Note: Each plate is accompanied by brief legends in English, French and Spanish. The plates are the same as in the German edition.

MARTIN, ÉMILE HIPPOLYTE, 1837-1891: Atlas d'ophthalmoscopie, accompagnées de considérations générales sur les altérations profondes de l'oeil visibles à l'ophthalmoscope, de tableaux symptomatologiques résumés, d'une échelle typographique et d'une table logarithmique pour la mésure des angles visuels . . . Paris, J. B. Baillière et Fils, ©1865. 31 pp., 4 tab., 8 col. pl.

Note: The illustrations, reproductions of paintings by the author, are crude and lacking in detail.

MARTIN, W. A.: *see* Jaeger, E. R.

MARZIO, QUIRINO DI, 1883-1954: Fundus oculi; diagnostica oftalmoscopica del . . . [Torino, Rosenberg & Sellier, 1937]. 5 p.l., 151 ll., 100 pl., 212 col. illus. Original edition in Italian.

Note: This is the most beautiful of the atlases of ophthalmoscopy and the first to be published in Italy. The figures are reproduced from original oil paintings by Miss A. Maggioli, who made her observations with the Gullstrand ophthalmoscope. The fundus pictures are not only faithful reproductions but also are remarkable examples of the printer's art.

———: Fundus Oculi; ophtalmoskopische Diagnose . . . Uebersetzung von E. B. Streiff . . . Torino, Rosenberg und Sellier, 1941. 16 p.l., 145 l., 100 pl., 212 col. illus. English

edition of text by Girolamo Bonaccolto (in pocket). 14 p.l., 103 pp.

MASSELON, J.: *see* Wecker, L. de.

MENIER (DE DECAZEVILLE): *see* Lagrange, F.

MONTMÉJA, A. DE: Pathologie iconographique du fond de l'oeil. Traité d'ophthalmoscopie, comprenant la théorie, la description et le maniement des divers ophthalmoscopes, l'étude du fond de l'oeil normal et pathologique, un atlas de 40 sujets dessinées et coloriés d'après nature. Paris, H. Lauwereyns, 1870. 4 p.l., 48 pp., 10 pl. in col.

NANO, HÉCTOR M.: Fundus oculi; patologia clinica vasculo retiniana, atlas, con 241 ilustraciones incluyendo 75 en color. Buenos Aires, 1953. 550 pp., 1 l.

Note: This is a comprehensive text with extensive bibliography. The illustrations, although not as true to life as some of those in recent European atlases, are entirely adequate for teaching, the purpose for which they were intended.

———: Fundus oculi; patologia clinica vasculo retiniana, atlas, con 312 ilustraciones incluyendo 105 en color. Ed. 3. Buenos Aires, Editorial Universitaria, Oscar Macchi, 1958. 748 pp., 305 illus., many in color.

NICOLAS, EUGÈNE, 1867- : Précis d'ophtalmoscopie vétérinaire par E. Nicolas et C. Fromaget. Paris, J. B. Baillière et Fils, 1898. viii, 120 pp., 9 col. pl.

Note: This is the first French work on veterinary ophthalmoscopy. It stresses the diseases of the eye of the horse. Seven of the colored plates illustrate the normal and diseased fundi of this animal which at that time had so much military importance.

OATMAN, EDWARD L., 1853-1913: Diagnostics of the Fundus Oculi . . . Troy, New York, the Southworth Co., ℗1913. 3 v., illus. One vol. of text with 234 illus., and 4 col. pl. and 2 portfolios with 79 stereograms and 8 diagnostic cards.

Note: The drawings reproduced of the pathologic specimens in volume 1 and the stereoscopic paintings reproduced in volumes 2 and 3 are by the author. This is the only atlas of stereoscopic paintings of the fundus that has been published. It is beautifully executed.

OELLER, JOHANN NEPOMUK, 1850-1932: (Atlas der Ophthalmoskopie). Atlas of Ophthalmoscopy. By Dr. J. Oeller . . . The text translated into English by Dr. A. H. Knapp . . . Wiesbaden, J. F. Bergmann, 1896-1899. 2 v., col. pl., bilingual text. (Issued in parts at irregular intervals.)

Note: This is the "elephantine" of the ophthalmoscopic atlases and for its time the most magnificent. Oeller painted pictures of the ocular fundi in oil on canvas. They are reproduced here.

———: Atlas seltener ophthalmoskopischer Befunde, zugleich Ergänzungstafeln zu dem Atlas der Ophthalmoskopie . . . Wiesbaden, J. F. Bergmann, 1900-1905. Folio unpaged, col. pl., German and English texts. (Issued in parts at irregular intervals.)

———: Atlas seltener ophthalmoskopischer Befunde, zugleich Ergänzungstafeln zu dem Atlas der Ophthalmoskopie. The text translated into English by Thomas Snowball. Wiesbaden, J. F. Bergmann, 1900-1924. 9 pts., fol. (Issued in parts at irregular intervals.)

PAVIA, JUSTO LIJÓ: Fondo de ojo a la luz de sodio (luz amarilla). El Atenio, 1941. 199 pp., 101 illus.

PERKINS, E. S., and HANSELL, PETER: An Atlas of Diseases of the Eye. With a Foreword by Sir Stewart Duke-Elder. Boston, Little, Brown and Co., 1957. ix, 91 pp., 105 col. illus.

Note: Many of the illustrations of the ocular fundus are in color.

PERRIN, MAURICE CONSTANTIN, 1826-1889: Traité pratique d'ophthalmoscopie et d'optométrie. Paris, G. Masson, 1870-1872. 2 v. Text, iv, 489 pp.; Atlas, 24 l., 24 pl., 17 pl. type. The Atlas volume has its own title page as follows: Atlas d'ophthalmoscopie et d'optométrie . . . composé de 24 planches en chromolithographie, comprenant 124 figures dessinées d'après nature et d'une échelle typographique disposée en 17 tableaux . . . Paris, Victor Masson et Fils, n.d.

Note: The colored plates in the atlas are pasted on appropriate pages, and were from water colors painted by Felix Regamey. A relatively large proportion of the text deals with the diagnosis of refractive errors.

———: Atlas des maladies profondes de l'oeil, comprenant l'ophthalmoscopie par M. Perrin et l'anatomie pathologique par F. Poncet . . . Paris, G. Masson, 1879. 98 l., 98 pl.

PILLAT, A.: *see* Dimmer, F.

PONCET, F.: *see* Perrin, M. C.

PRESSBURGER, E.: *see* Fuchs, A.

RENARD, GABRIEL: . . . Aspects pathologiques du fond de l'oeil dans les affections de la rétine. Atlas ophtalmoscopique I. Rapport présenté à la Société française d'ophtalmologie le 21 Mai 1946 . . . Paris, Masson et Cie, 1946. 170 pp., illus., 32 col. pl.

Note: In this volume only the diseases of the retina are considered. The colored reproductions are from paintings by Mlle. E. Lalau.

DE RIVAS CHERIF, MANUEL: La fotografía de las membranas profundas del ojo. [México, D. F.], La Casa de Español en México [1940]. 1 l., 75 pp., illus.

ROLLET, ÉTIENNE, 1862-1937: Traité d'ophthalmoscopie . . . Paris, Masson et Cie, 1898. ix, 379 pp., 50 col. pl.

ROUTIER, DANIEL: Le fond d'oeil, des hypertendus, et des cyanosés. Paris, Masson et Cie, 1947. viii, 100 pp., 232 figs. in plates.

Note: The illustrations are black-and-white photographs of uneven quality. Routier is a cardiologist, and the book is written from the viewpoint of his specialty.

RUETE, C. G. THEODORE, 1810-1867: Bildliche Darstellung der Krankheiten des menschlichen Auges. 1. u 2. Lfg. Physikalische Untersuchung des Auges . . . Leipzig, B. G. Tuebner, 1854-1866. 6 v. in 9 pts., illus.

Note: Parts 1 and 2 published in 1854 include a comprehensive account of the ophthalmoscopes of Ruete, Helmholtz, Coccius and Meyerstein. There are also descriptions of the eyegrounds. The fundi are represented by 24 examples of normal conditions and of disease. The retina is shown in the pupillary area and the iris and lids are drawn in detail. The illustrations are hand-colored on black-and-white copper engravings. The plates are signed by Loedel, who not only was the engraver but probably the artist also. (See frontispiece of this brochure.)

SALZMANN, M.: *see* Jaeger, E. R.

SANZ ASTOLFI, J.: *see* Uribe y Troncoso, M.

SAUTTER, HANS: *see* Marchesani, O.

SCHAUENBURG, C. H.: *see* Van Trigt, A. C.

SCHLOSSMAN, A.: *see* Fuchs, A.

DESCHWEINITZ, G. E.: *see* Haab, O.

SIEGERT, PETER: . . . Auge und Allgemeinerkrankungen. Einführende Vorlesungen zum Augenspiegelkurs. Hamburg, H. H. Nolke, 1944. 104 pp., illus.

———: . . . Augenspiegelkurs. Der normale und pathologische Augenhintergrund; Anhang: Gesichtsfeldstörungen. [2 Aufl.] Hamburg, H. H. Nolke, 1945. 131 pp., illus.

———: . . . Vorlesungen über Augenheilkunde. Augenspiegelkurs; der normale und pathologische Augenhintergrund; Anhang: Gesichtsfeldstörungen . . . 3 Aufl. Hamburg, H. H. Nolke, 1947. 2 p.l., v, 131 pp., illus.

Note: The third edition is printed on very poor paper, for which the author apologizes. The illustrations consequently are blurred reproductions of what were probably good photographs.

SNOWBALL, T.: *see* Oeller, J. N.

STREIFF, E. B.: *see* Marzio, Q. di

SWANZY, H. R.; *see* Liebreich, R. L.

SZILI, AUREL [ADOLF], 1848-1920: Augenspiegel-Studien zu einer Morphographie des Sehnerven—Sintrittes im menschlichen Auge. Wiesbaden, J. F. Bergmann, 1901. I. Tafeln. 92 pp., 24 pl.

Note: Detailed study of the optic nerve head, especially in regard to the physiologic cup and scleral crescents.

SZYMÁNSKI, JULIUS: Corpus tabularum ophthalmicarum. Tab. I. Nervus opticus et retina. Tab. II. Iris et choroidea. Tab. III. Cornea. Wilno, Joseph Zawadzki, 1930. 22 pp., 4 col. pl., 2 black-and-white pl.; total of 120 figs. English text.

TASSMAN, ISAAC SAMUEL, 1892- : The Eye Manifestations of Internal Diseases. 201 illus., including 19 in color. St. Louis, The C. V. Mosby Company, 1942. 3 p.l., 5-542 pp., illus.

———: The Eye Manifestations of Internal Diseases. Ed. 2. . . . St. Louis, The C. V. Mosby Company, 1946. 614 pp., 243 illus.

———: The Eye Manifestations of Internal Diseases. Ed. 3. St. Louis, The C. V. Mosby Company, 1951. 672 pp., 279 illus., 25 in col.

Note: The emphasis here is not so much on the eye itself as on the diseases that may manifest themselves in the eye. It is a valuable current text.

TERSON, A.: *see* Haab, O.

THIEL, RUDOLF: Atlas der Augenkrankheiten; Sammlung typischer Krankheitsbilder mit kurzen diagnostischen und therapeutischen Hinweisen; mit 420 meist farbigen Abbildungen. Leipzig, Thieme, 1937. 196 pp. (figs. 272-420 are of the fundus—col.).

———: Atlas der Augenkrankheiten, Sammlung typischer Krankheitsbilder . . . mit 634 meist farbigen Abbildungen. 2 Aufl. Leipzig, Georg Thieme, 1941.

Note: The original could not be consulted.

———: Atlas der Augenkrankheiten . . . 3 Aufl. mit 634 meist farbigen Abbildungen. Leipzig, Georg Thieme, 1943.

Note: The original could not be consulted.

———: Atlas der Augenkrankheiten . . . 4 Aufl. mit 634 meist farbigen Abbildungen. Leipzig, Georg Thieme, 1947.

Note: The original could not be consulted.

———: Atlas der Augenkrankheiten, Sammlung typischer Krankheitsbilder mit kurzen diagnostischen und therapeutischen Hinweisen . . . 5 Aufl, mit 634 meist farbigen Abbildungen. Stuttgart, Georg Thieme, 1948. 4 p.l., 225 pp. (figs. 430-585 are of the fundus—in col.).

Note: This volume includes excellent illustrations of diseases of all parts of the eye. A third of the book is devoted to the fundus and depicts in color most of the usual intra-ocular diseases.

THORINGTON, JAMES, 1858-1944: The Ophthalmoscope and How to Use It. With Colored Illustrations, Descriptions, and Treatment of the Principal Diseases of the Fundus. Philadelphia, P. Blakiston's Son and Co., 1906. xi, 298 pp., illus., 12 pl. in col.

Note: While primarily a manual, this volume is included since it contains 12 colored plates of the fundi. The original sketches in color were prepared by Margaretta Washington, under the direction of the author.

TILLÉ, HENRI, 1901- : Atlas clinique d'ophtalmoscopie photographique, syndromes cliniques du fond de l'oeil (Clinical Atlas of Photographic Ophthalmoscopy) par Henri Tillé . . . et A. Couadau. Paris, Masson et Cie, 1939. 1 p.l., 193 pp., 196 photographs.

Note: This volume is devoted in large part to eye changes in cardiovascular-renal diseases. The illustrations are photographs in black and white taken with a Zeiss reflex-free camera.

TOWER, PAUL: Differential Diagnosis of Common Diseases of the Eyeground . . . xi, New York, Grune & Stratton, 1953. 243 pp., 129 pl.

Note: This compact, practical little volume is arranged especially for teaching. The photographs of the fundus are not reproduced as faithfully as would be desirable.

TRIGT, A. C. VAN: *see* Van Trigt, A. C.

URIBE Y TRONCOSO, MANUEL, 1867-1959: Internal Diseases of the Eye and Atlas of Ophthalmoscopy . . . illustrated with 239 engravings including 95 figures on 82 full-

page color plates. Philadelphia, F. A. Davis Co., 1937. xxii, 530 pp., pl. (Partly col., 1 folding), diags.

Note: This is a modern text and stresses the pathogenesis of diseases; it is complete and well organized. The better illustrations are largely selected from other publications.

———: Internal Diseases of the Eye and Atlas of Ophthalmoscopy . . . Ed. 2. Philadelphia, F. A. Davis Co., 1950. xviii, 648 pp., illus., 94 pl. in col.

———: Enfermedades internas de los ojos y atlas de oftalmoscopia . . . Traducida al español de la segunda edicion en ingles por el Dr. Joaquin Sanz Astolfi . . . Mexico [D.F.], Editorial Interamericana, S.A., 1952. xx, 736 pp., 1 l., 189 illus. in black and white, 92 in col.

Note: The Spanish translation was published in Mexico in 1952.

VAN TRIGT, ADRIAN CHRISTOPHER, 1825-1864: Dissertatio ophthalmologica inauguralis de speculo oculi . . . Traj. ad Rhenum, P. W. van de Wecjer, 1853. 87 pp., 1 fold. pl., 3 col. pl.

Note: This thesis, written when the author was 23 years of age, contains the first printed illustrations of the fundus of the eye. They are in color and skillfully drawn.

———: Der Augenspiegel und seine Anwendung und Modificationen, nebst Beiträgen zur Diagnostik innerer Augenkrankheiten. Nach dem Holländischen mit Zusatzen bearb. von C. H. Schauenburg . . . Lahr, J. H. Geiger, 1854. xiii, 125 pp., 2 l.

———: Der Augenspiegel und seine Anwendung und Modificationen, nebst Beiträgen zur Diagnostik innerer Augenkrankheiten. Nach dem Höllandischen . . . mit Zusatzen bearb. von C. H. Schauenburg . . . 2 Aufl. Lahr, M. Schauenburg and Co., 1859. xv, 110 pp., 2 col. pl.

WECKER, LOUIS DE, 1832-1906: Ophthalmoscopie clinique par Louis Wecker et J. Masselon, avec 40 photographies hors texte. Paris, Octave Doin, 1881, iii, 5-256 pp., illus.

———: Ophthalmoscopie clinique par L. de Wecker et J. Masselon . . . 2 ed. Paris, Octave Doin, 1891. 3 l., iii, 399 pp., 40 pl.

———: Traité des maladies du fond de l'oeil et atlas d'ophthalmoscopie, par L. de Wecker et de Jaeger. Paris, A. Delahaye; Vienne, Imprimerie Impériale et Royale, 1870. 2 v. in 1, illus., 29 col. pl.

Note: The text is by de Wecker and utilizes Jaeger's colored plates for illustrations.

WILMER, WILLIAM HOLLAND, 1863-1936: Atlas Fundus Oculi. Introduction by Warfield T. Longcope. New York, Macmillan, 1934. 39 pp., 100 col. pl.

Note: This is a collection of 100 reproductions of paintings of the fundus of the eye by Mrs. Annette S. Burgess from clinical material encountered at the Wilmer Institute.

WOLFE, J. R.: *see* Magnus, H. F.

WOOD, CASEY ALBERT, 1856-1942: The Fundus Oculi of Birds, Especially as Viewed by the Ophthalmoscope; a Study in Comparative Anatomy and Physiology . . . Illustrated by 145 drawings in the text; also by 61 colored paintings prepared for this work by Arthur W. Head . . . Chicago, the Lakeside Press, 1917. 3 p. l., 5-180 pp., illus., col. pl.

Note: Casey Wood made a comprehensive study of the ophthalmoscopic appearance of eyes of birds. Ornithology was a lifelong hobby of the author. The colored plates are by A. W. Head.

YAMADA, TOKUSHI: Kengankio yohio (The Method of Using the Ophthalmoscope). Tokio, 1881. 13 pp., 336 pp., 5 pl. in col. Japanese text.

Note: There seems to be only one copy of this Japanese work in the United States, in the National Library of Medicine. The illustrations are poor.

YANES, TOMÁS R.: Manual de oftalmoscopia clínica . . . Habana, Biblioteca Médica de Autores Cubanos, 1943. 500 pp., illus., 14 col. pl., references pp. 485-496.

Note: The colored plates are copied from Oeller; the figures from standard North American texts.

THE EFFECTS OF PHYSIOLOGIC BALANCED SALT SOLUTIONS AND NORMAL SALINE ON INTRAOCULAR AND EXTRAOCULAR TISSUES

D. L. Merrill, M.S., and T. C. Fleming, M.A.
Fort Worth, Texas

and

Louis J. Girard, M.D.
Houston, Texas

The use of tissue culture as an investigative tool is becoming increasingly popular in the study of drug preparations. One of the reasons is that the destructive effects of drugs can be studied on growing tissue at the cellular level in a controlled medium.

For many years ophthalmologists have used solutions of normal saline for irrigating the intraocular and extraocular tissues during surgery. Recent methods of testing the toxic properties of various chemical solutions on cultures of human tissues have provided us with a method of evaluating these solutions to a low degree of toxicity.

Pomerat and Overman[1] have shown that cellular damage resulted from saline perfusion on tissues from the human nasal mucosa. Shambaugh[2] has shown that saline solutions were injurious to cells cultivated from the organ of Corti and from the middle ear mucosa of the cat. Harper and Pomerat[3] reported the effects of various electrolyte mixtures on cells obtained from rabbit cornea and human conjunctiva using time-lapse cinematography.

Girard, et al.,[4] reported evidence of toxicity to explants of human conjunctiva when perfused with normal saline. Fleming, Merrill and Girard[5] have shown that by intraocular injections of methylcellulose prepared in a balanced salt solution no evidence of iritis resulted in animal studies, whereas injections of methylcellulose prepared in 0.9-percent sodium chloride resulted in a mild iritis.

The purpose of the work reported in this paper was to study further the effects of normal saline and a balanced salt solution in animal eyes simulating the irrigation of the intraocular tissues by the ophthalmologist and to study its effects on other tissues of the eye in vitro.

Materials and Methods

The specimens of human tissue were obtained from patients undergoing surgical operations for cataract, muscle and ptosis correction, and iridectomies. Iris and conjunctival tissues were used in this study. The conjunctival tissues were carefully removed from the eye in order not to obtain tissue of Tenon's capsule. All tissues were placed in sterile Gey's balanced salt solution immediately after removal from the subject.

Explants of tissue measuring approximately one mm.^{2} were placed on a sterile cover slip and embedded in a clot consisting of equal parts of heparinized cockerel plasma and chick embryo fluid. When the clot was firmly set, the clotted tissue was placed in a sterile perfusion chamber which was then filled with fluid nutrient of 20-percent pooled normal human serum, Hanks balanced salt solution and amino acid concentrate. The tissues were permitted to grow in this medium from two to five days with changes of the medium when necessary. Time-lapse cinematography, utilizing the AO Baker interference microscope, was employed as the method of recording the action of the various solutions on the growing cells.

Solutions employed in the study were two balanced salt solutions and an 0.9-percent sodium chloride solution. The two balanced salt solutions were (a) Hanks solution, and (b) a commercial balanced salt solution. Each

TABLE 1

COMPOSITION (GM./100 ML.) OF TEST SOLUTIONS

Component	Hanks BSS	BSS "A"*	Normal Saline
NaCl	0.8	0.49	0.9
Glucose	0.1		
KCl	0.04	0.075	
$MgSO_4 \cdot 7H_2O$	0.02		
$MgCl_2 \cdot 6H_2O$		0.030	
$KH_2PO_4 \cdot 12H_2O$	0.006		
$Na_2HPO_4 \cdot 2H_2O$	0.006		
$CaCl_2$	0.014	0.036	
CH_2-COONa		0.39	
$2Na_3C_6H_5O_7 \cdot 11H_2O$		0.17	
$NaHCO_3$	0.025		
Phenol Red	0.002		
pH	6.9	7.2	7.0

All solutions were prepared in triple distilled water.
* Listed as solution "A" by Harper and Pomerat.[3]

solution used was prepared in triple distilled water and then filtered through a sintered glass filter and autoclaved for 15 minutes at 121°C. (15-17 lb./in² steam). The cells were perfused for 30 to 35 minutes with each of the three solutions. The composition of these three solutions is given in Table 1. All time-lapse studies were taken at eight frames per minute. After a 35-minute perfusion period with the test solution, the tissue culture medium (20-percent mixed human serum, Hanks balanced salt solution and amino acid concentrate) was used in an attempt to revive those tissues where toxic manifestations were noted.

Animal studies consisted of three series of experiments using 13 albino rabbits. Only animals which showed no evidence of previous surgery or infections were used in the study. The three solutions were prepared aseptically and were administered by perfusion of the anterior chamber with the solutions.

The animals were sedated with Nembutal, given a retrobulbar injection of 0.5 ml. of procaine (two percent) and two drops of tetracaine were instilled in the conjunctival sac. After a five-minute interval the eyes were flushed with the balanced salt solution to remove any drug from the surface of the conjunctiva and cornea. By use of a keratome, an oblique corneoscleral section was made to receive the irrigating cannula and permit the flow of solution to leave the anterior chamber freely. The anterior chamber of each animal eye was irrigated with 25 cc. of the irrigating solution during a period of five to six minutes. After this period, the corneoscleral flap was closed and slitlamp biomicroscopic observations were made of each animal on a daily basis for a period of 10 days.

RESULTS

Cinemicrographic records of explants of human conjunctiva and iris perfused with the test solutions were studied using Kodachrome Type A film. The perfusion studies indicated the following results. Neither Hanks nor the BSS "A" balanced salt solutions produced any indication of toxicity to growing cells (conjunctiva or iris) during the 35-minute period of perfusion. According to previous studies[5] and the referenced work of others, criteria of toxicity for cells in tissue culture exposed to toxic concentrations of a drug have been found to be: (a) retraction of the cell membranes and cytoplasm; (b) rapid agitation of the cells followed by halting of cellular movement; (c) halting of intracellular movement; (d) vacuole formation; (e) boiling or bubbling of cytoplasm; and (f) rupture of the cell membrane and death of the cell.

Perfusion of the explants with 0.9-percent sodium chloride solution showed the following: The cells of the explant began to show rapid movement after three to five-minute exposure. There followed rapid retractions of the cytoplasmic processes, and after a short period, impairment of cellular movement became apparent. In some experiments, all intracellular and cellular movement ceased after a 35-minute interval of exposure. After several hours of perfusion with the original tissue medium, the cells were revived and normal cell function resumed.

The results of the in vivo studies in animals seemed to corroborate the findings in tissue culture. After perfusing the anterior

TABLE 2

THE BIOMICROSCOPIC EFFECTS OF HANKS BALANCED SALT SOLUTION, A COMMERCIAL BALANCED SALT SOLUTION AND 0.9-PERCENT SODIUM CHLORIDE FOLLOWING IRRIGATION INTO THE ANTERIOR CHAMBER OF ALBINO RABBITS

Animal	Type Solution	Number Days before Clearing
1. O.S.	Hanks	2
O.D.	0.9% NaCl	5
2. O.S.	Hanks	2
O.D.	0.9% NaCl	6
3. O.S.	Hanks	1
O.D.	0.9% NaCl	4
4. O.S.	Hanks	2
O.D.	0.9% NaCl	7
5. O.S.	BSS "A"	2
O.D.	0.9% NaCl	6
6. O.S.	BSS "A"	2
O.D.	0.9% NaCl	4
7. O.S.	BSS "A"	2
O.D.	0.9% NaCl	4
8. O.S.	BSS "A"	1
O.D.	0.9% NaCl	6
9. O.S.	BSS "A"	1
O.D.	0.9% NaCl	6
10. O.S.	BSS "A"	3
O.D.	0.9% NaCl	9
11. O.S.	BSS "A"	2
O.D.	0.9% NaCl	10
12. O.S.	BSS "A"	1
O.D.	0.9% NaCl	7
13. O.S.	BSS "A"	2
O.D.	0.9% NaCl	7

chambers with the test solutions, biomicroscopic examinations at daily intervals showed that all eyes had some clouding of the cornea and turbidity of the aqueous, initially. The rate, however, of disappearance of these signs differed greatly according to the test solution used (table 2). Clearing of the cornea and aqueous after perfusion with Hanks solution averaged 1.75 days in four animals; the eyes perfused with BSS "A" averaged 1.88 days in nine animals. Thirteen eyes perfused with 0.9-percent sodium chloride, however, averaged 6.2 days in clearing of the cornea and aqueous after exposure to the solution.

DISCUSSION

The intraocular fluid of the eye contains some seven different ions, globulins and albumin fractions, organic and amino acids, and proteolytic enzymes;[6] with the tissues of the internal structures being constantly bathed in this fluid. Changes in this solution result in severe changes of the various salt balances within the eye with an abnormal effect resulting. The pH of the aqueous humor was found to be around 7.53 by von Sallmann and di Grandi.[7] The pH of the three solutions used in this study ranged from 6.9 to 7.2. It is not unreasonable to assume that a solution containing only two ions would not be an ideal preparation to which the delicate tissues of the eye should be subjected; this would produce ionic imbalance with resultant trauma at the tissue level.

The results of irrigating the anterior chamber of the animal eye indicate that this ionic imbalance is extant and that additional trauma results. The sodium chloride solution did not in any case give similar results to the two balanced salt solutions. The recovery period, in days, indicated that the two balanced salt solutions did not damage the intraocular tissue, and the one to three day recovery period for eyes receiving these two solutions could have been caused by the surgical trauma necessary to enter the anterior chamber for the irrigation. The extended damage beyond this period would indicate damage to the cells by the solutions.

CONCLUSIONS

Three so-called physiologic solutions were tested for their damaging effect on tissues obtained from the human eye as well as in vivo studies on intraocular tissues of albino rabbits. The two balanced salt solutions did not damage the intraocular tissues, whereas, 0.9-percent sodium chloride solution showed damage to tissues both in vivo and in vitro.

P.O. Box 1959.

Hermann Professional Building (25).

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SPONTANEOUS CHOROIDAL DETACHMENT*

Report of two cases

C. M. J. Velzeboer, M.D.
Amsterdam, Holland

Secondary detachment of the choroid is frequently encountered after eye operations, especially after cataract extraction and trephination. Its development has been discussed by various authors. Fuchs' original theory was that it results from fluid from the anterior chamber oozing through a cleft in the ciliary body. Chemical analysis of the fluid (Hagen) showed that it must be a transudate from the vessels of the ciliary body. A prolonged leakage from the anterior chamber causes the vitreous to exude fluid. Decrease of the vitreous volume causes a negative pressure in the globe and congestion and transudation of the ciliary vessels in the presence of a rigid sclera. Usually the condition has a favorable course. Once the depth of the anterior chamber and the intraocular pressure have become normal, the detachment generally decreases. Occasionally pigmentary streaks are observed at the border of the original detachment.

Contrary to secondary detachment of the choroid, primary spontaneous detachment is rare. The first known cases were described by von Graefe in 1858. Recently (1954) Hertz has reviewed the literature, covering 90 cases. From this review it is evident that spontaneous choroidal detachment is not a clinical entity but rather a symptom that may be encountered in various pathologic eye conditions. Of the 90 cases described, 23 refer to sudden hypotonia in retinal detachment with a deep anterior chamber, the eye being slightly injected. According to Gonin, if such symptoms complicate the picture of retinal detachment, choroidal detachment should be suspected.

Omitting these hypotonic cases, a group of spontaneous cases are left in which ocular tension is normal, the depth of the anterior chamber is generally normal, and the etiology frequently unknown. All the cases have in common the symptoms of choroidal detachment, a circumferential dark-rose prominence is seen in the peripheral part of the fundus, with three or four indentations at the points of entry of the v. vorticosae. The suprachoroidal space is filled up with fluid. This suprachoroidal space is a cleft with strands of very loose connective tissue in the periphery; centrally the choroid is more firmly attached to the sclera and here no choroidal detachment occurs. The dark color excludes a diagnosis of retinal detachment. In some cases there may also be some subretinal fluid, as with my first patient. In dia-

* From the University Eye Hospital. Director: Prof. Dr. A. Hagedoorn.

scleral illumination, owing to a subscleral cavity filled with fluid, the shining area of the sclera is larger than it would be normally (Hagen's symptom). Moreover, in diascleral illumination not only retinal but also choroidal vessels can be seen in the detached area (fig. 1). Apart from the detachment there may be other symptoms, varying from patient to patient.

Case reports

Case 1

A woman, aged 48 years, was referred to the University Eye Hospital in August, 1954. She complained that during the previous six days she had been having haziness of vision in the right eye.

Eye examination. Vision of the left eye was 5/4, emmetropia, no abnormality; of the right eye, 1/300, no correction. Anterior segment: no abnormality. The vitreous showed some opacities. In the fundus an extensive grayish-rose colored detachment occupied the whole periphery, with four constrictions at the points of the v. vorticosae (fig. 2). More centrally in the superior part there was a less prominent white retinal detachment. The retinal vessels and optic disc were normal. No retinal tear was found.

The diagnosis of choroidal detachment was made because of the aspect of the detachment—its color, its well-defined and motionless outlines and the fact that diascleral illumination excluded the possibility of tumor. The tension was normal. The visual field was limited to a small field in the upper part.

General examination. For the past 10 years the patient had been suffering from chronic rheumatism. Slight atrophy of the muscles of the hands, with contractures, was found. During the preceding eight years she had been receiving gold treatments; before admittance she was given 25 mg. aureomyesine (Solganol) intramuscularly every fortnight. After admittance the dose was given three times and the gold treatment was then discontinued. The sedimentation rate of 7/15 rose to 41/76. The blood count was normal. Her secondary sexual characteristics were underdeveloped. She had never menstruated.

Fig. 1 (Velzeboer). Picture in diascleral illumination. Large shining area is the sclera. In the pupil can be seen pigment streaks in the region of the ora serrata.

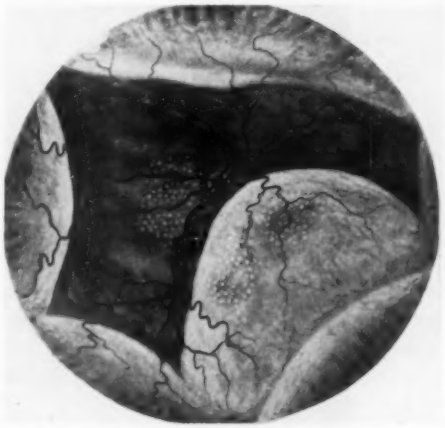

Fig. 2 (Velzeboer). *Case 1,* right fundus.

Family history. One sister suffered from neurofibromatosis.

Course. During three weeks of immobilization, the condition improved only slightly. On September 16th, after the aspiration of 0.5-cc. subchoroidal fluid, an electrocoagulation was performed in the nasal superior region. Analysis of the fluid gave the following data: Nonne and Pandy positive, 58.1‰ protein, 1.25‰ glucose, threads of fibrin, fragments of cells.

There was practically no change three days after the operation. A second operation was performed on October 7th—a posterior trephination surrounded by a field of electrocoagulation. A great deal of fluid drained off. Salt solution was injected into the anterior chamber, causing a hemorrhage which cleared up after several days, leaving one posterior synechia. The fundus picture remained unchanged; the retinal detachment alone was improved.

The patient was dismissed on December 7th. During the succeeding months the choroidal detachment remained unchanged. In the central part of the retina pigmentary changes developed. The retinal pigment layer became atrophic, with clots of pigment (fig. 3). This pigment maceration increased from the central region to the periphery. On examination in July, 1955, the choroidal detachment had suddenly disappeared, though some subretinal fluid persisted in the inferior part; however, this also disappeared during the two succeeding weeks. By this time there were pigmentary changes throughout the whole of the fundus. The retinal arteries grew thin. Light projection was intact; vision,

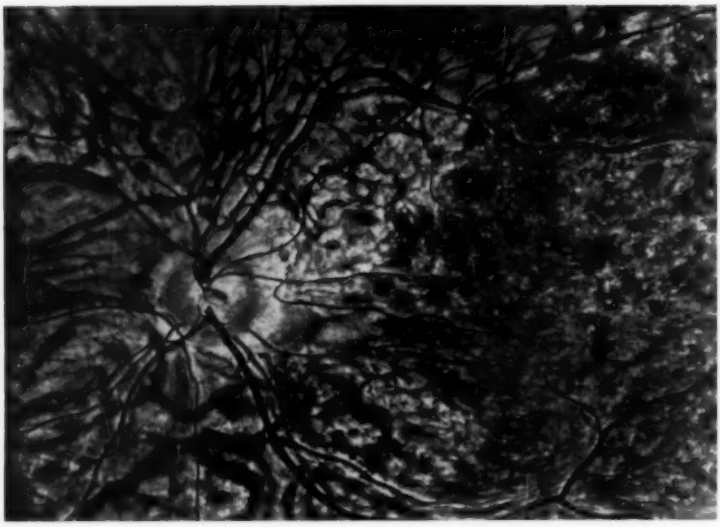

Fig. 3 (Velzeboer). Clotting of the pigment epithelium in the right fundus in Case 1.

finger counting; visual field, a small paracentral rest. The anterior chamber was consistently clear and of normal depth. The ocular tension was normal. During the whole course of observation the left eye showed no abnormality. The condition of the right eye has so far remained unchanged. A recent electroretinogram (February, 1958) of the right eye was negative, of the left eye normal.

CASE 2

A woman, aged 65 years, suffered from red and slightly painful eyes. In January, 1956, her ophthalmologist, Dr. Mesker, diagnosed episcleritis. At that time no further particulars were found in the eyes. Vision was: R.E., 1(S + 5); L.E., 1(S + 5). There was a history of general malaise during the preceding year, with a period of fever. In June, 1956, the patient was seen again by Dr. Mesker in the outpatient department of the University Eye Hospital.

Eye examination. The right eye was slightly injected and the anterior chamber was opalescent, with a few small corneal precipitates. Iris was clear. There were no posterior synechias. Lens and vitreous were clear. Ophthalmoscopy showed a dark, grayish prominence occupying the whole periphery; it was divided into four parts, the nasal and superior parts being the largest. Temporally and inferior and more centrally the retina was detached and slightly prominent. A diagnosis of choroidal detachment together with retinal detachment in the inferior temporal quadrant was made. Intraocular pressure was normal. Vision and refraction were unchanged.

Course. Two weeks later control investigation showed that the choroidal as well as the retinal detachment had completely vanished. There continued to be periods of episcleritis. In November, 1956, the patient was admitted to the Internal Medicine Clinic (Prof. Borst) for general investigation. She had vague complaints of abdominal pains. On admittance her temperature was 38.5°C. but during the succeeding weeks it became normal. The sedimentation rate of 125/135, defibrinated 32/69, decreased to 60/92. Blood: leukocytosis (10,000); for the rest, normal. Only during the first days the spleen was palpable. No diagnosis could be made.

The latest investigation, in October, 1957, revealed no injection in either eye, clear media. In the right fundus were pigmented streaks in the region of the recent detachment, and there were slight pigmentary changes in the macular region such as in senile macular degeneration. Vision was: R.E., 0.5; L.E., 5/5. The fundus of the left eye was normal.

COMMENT

It has already been noted that spontaneous choroidal detachment is not a clinical entity and may have various etiologies. One of these may be a hemorrhage, especially after a trauma.

Gilbert subdivides choroidal detachment into two groups: (1) cases with low tension, in which the shrinking of the vitreous is basic; (2) cases with normal or elevated tension, in which transudation or exudation are more important.

In my two patients both the tension and

the anterior chamber were always normal, therefore shrinkage of the vitreous could not have been a causative factor.

Reported in the literature are cases with no ocular inflammation but frequently accompanied by retinal detachment (Weve, Law and, possibly, Stallard's cases of annular detachment, strongly suggestive of complicating choroidal detachment). In other cases there were inflammatory signs varying from mild irritation (Rohrschneider, posterior synechias) to severe inflammation, such as in Dollfus' case, with chemosis, impairment of eye movement, scleritis and tenonitis. In his case the eye was enucleated and pathologic-anatomic investigation revealed subacute choroiditis. In my second patient, there were distinct signs that the choroidal detachment might have been caused by an inflammation, possibly scleritis. In this patient no puncture for subchoroidal fluid was made. No etiology of the intraocular inflammation can be given. A thorough internal examination gave no help in finding a causative agent.

There were no inflammatory reactions in the eyes of my first patient, although the general condition, chronic rheumatism, may easily be taken as a mild and localized septic focus. Chemical and cytologic investigation of the subchoroidal fluid revealed a relatively high protein content, threads of fibrin, and only fragments of cells. This might explain transudation but might just as easily be expected in an exudation with very few cells. As a matter of fact the distinction between transudation by alteration of the vascular wall and exudation is extremely vague. It is impossible for us to make a choice between the two, although vascular changes concur with the long-delayed resorption. The detachment remained unaltered for nearly a year.

Pigmentary changes

Pigment streaks are frequently seen after a choroidal detachment has disappeared. In one case alone, Stallard mentioned pigmentary changes of the whole retina following choroidal detachment. In my first patient pigment changes even started in the central parts, where there had been no detachment. The pigment was clotted but showed no bone-corpuscle structure. No sclerosis of the choroidal vessels was seen and no sign of inflammation or scars in the choroid.

The striking disturbance of the pigment epithelium and the neuro-epithelium (evident from the absence of the electroretinogram) together with secondary atrophy of the retinal vessels suggest secondary tapetoretinal degeneration. Identical changes in a group of patients after the application of piperidin-phenotiazine were described by Rintelen. In these cases the pigmentary changes increased after the drug was discontinued, although the function of the eye improved. In my first case the gold may have had a toxic effect, as was suggested by Zeeman. For eight years, however, the patient had been having gold therapy without any toxic signs, such as dermatitis, stomatitis, nephritis, or hepatitis, the first signs likely to appear.

The same fundus picture was described in patients after viral or bacterial infections. Recently (1958) Franceschetti reviewed a series of cases of secondary pigmentary degeneration of the retina in which viral infection was almost certainly causative. In most patients visual function was much disturbed. The electroretinogram was generally negative. The condition was invariably bilateral. Our patient had had no infectious disease since her childhood.

According to Fuchs and Wagenmann, retinal pigmentary degeneration may be due to a disturbance of the choriocapillaris. The influence of the choroidal circulation on the fundus picture was demonstrated experimentally by Wagenmann; dissection of one long ciliary artery and some of the short ciliary arteries caused pigmentary disturbance (clotting) in the retina, with regional atrophy of the choroid.

Zeeman drew attention to the possible role

of choroidal circulatory disturbances in various clinical pictures revealing pigmentary changes. Bailliart, in particular, has pointed out the role of the choriocapillaris in central retinal degenerative processes accompanied by atrophy of the pigment epithelium.

All this refers to the central area, the region of the short ciliary arteries; the network of the vessels were in a degenerative or inflammatory state. In my first case no changes in the choroidal vessels were to be seen. How far a long-standing alteration of the choroidal (ciliary) circulatory system may affect the retinal pigment layer is a question we must leave unanswered.

Prognosis

In cases of choroidal detachment and hypotonia, the prognosis is unfavorable and ultimate atrophy is to be feared. In cases of normal tension, like the ones herein reported, the prognosis is generally good. The detachment vanishes either spontaneously or after therapy, usually without loss of function, as in my second case. As a series of bilateral cases are described in the literature and affection of the second eye may only start many years after that of the first (in Verhoeff's case eight years), eventual involvement of the other eye must be taken into account. In neither of my own patients has the second eye so far shown any abnormality.

Therapy

At our hospital, in cases of postoperative total or almost total choroidal detachment posterior trephination is done in the detached region, with invariably good results.* In spontaneous choroidal detachment of long standing or progression, simple draining of the subchoroidal fluid may be done as a rule together with diathermic coagulation which is all the more indicated if there is also a retinal detachment. Good results from this procedure have been noted by others (Weve and Stallard). There may be a relapse after draining, as in my own and Rohrschneider's cases. In my first patient there was a relapse after trephination with diathermic coagulation; the detachment reappeared unaltered until, in its own good time, it vanished spontaneously. Rohrschneider had the same experience. In the final analysis it would seem to be a question of patience.

As the process by which choroidal detachment originates is still unknown, therapy cannot yet be directed to the cause.

Summary

Two patients with spontaneous choroidal detachment have been described, both unilateral cases.

In the first patient the detachment occurred with no signs of ocular inflammation and it failed to respond to surgical therapy. After 11 months it vanished spontaneously, leaving pigment maceration throughout the fundus and disturbed visual function.

In the second patient there were mild inflammatory signs. The choroidal detachment occurred after a period of recurrent episcleritis and vanished within two weeks, leaving no visual deterioration.

University Eye Hospital.

*Addendum

Dr. Crone did a cyclodialysis in a case of choroidal detachment with shallow anterior chamber. The chamber became normal and the detachment vanished (personal communication).

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THE CARE OF OPHTHALMIC SURGICAL INSTRUMENTS*

JOSEPH GEORGE ROSENBAUM, M.D.
New York

The purpose of this paper is to present a routine for handling ophthalmic surgical instruments based on the recognition of the qualities of surgical stainless steel in use today.

Stainless steel is an alloy which was created to resist corrosion. The presence of carbon, the quality of temper and the inclusion of other metals such as nickel, chromium, and so forth, will determine its classification. Most instruments used for eye surgery are now being made of steel of the so-called "400-series."†

Many ophthalmic surgeons are not yet aware of the quality or capacity of the steel alloys now being used and, therefore, of the ability of the cutting edges of the newer instruments to resist corrosion and dulling as was produced by heat and moisture when sterilizing the older types of steel.

Actually, the appreciation of these qualities would enable the surgeon to do away with the soaking techniques currently used in the sterilization of sharp instruments. The soaking technique has several disadvantages. (1) greater length of time needed for sterilization of "sharps" and (2) extra precautions needed for complete washing of the instruments with sterile water or saline solution prior to use.

Aside from the technique mentioned, a method will be described which minimizes the tedious process of sorting instruments for each case, does away with excess handling of instruments by personnel not cognizant of the extreme delicacy of instruments and modifies the washing and drying process which is responsible for most wear and tear of instruments.

STORAGE OF INSTRUMENTS

All stainless steel instruments for surgery of cataract, extraocular muscles, and enucleation are kept in marked muslin bags similar in design to bags used for storage of fine silver flatware, each slot being inscribed with laundry marking ink for identification of the instrument. One bag contains all the forceps (fig. 1), a second one contains all other instruments except those used for cutting (fig. 2), while the third holds the scissors (fig. 3).

* From the Department of Ophthalmology of the Bronx Municipal Hospital Center and the Albert Einstein College of Medicine of Yeshiva University, New York City. Trainee under USPHS Graduate Training Grant No. 2-B-5196(C1).

† Information referable to the ability of these steels to withstand the procedures described herein was generously supplied by metallurgists of Republic Steel Corporation, U.S. Steel Corporation, The Peter A. Frasse Company, and the Frank L. Crobaugh Company.

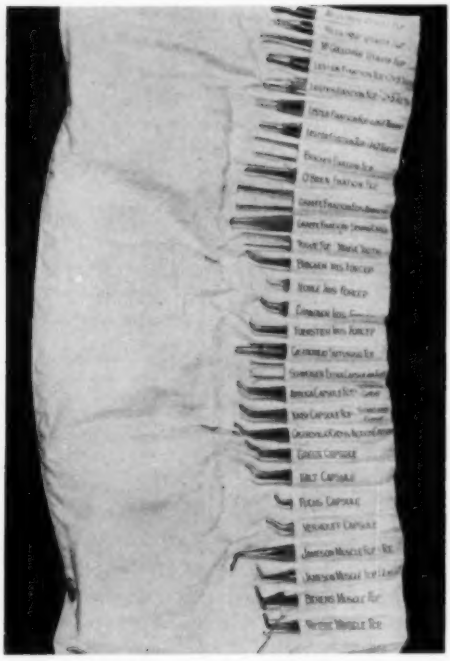

Fig. 1 (Rosenbaum). Bag containing forceps.

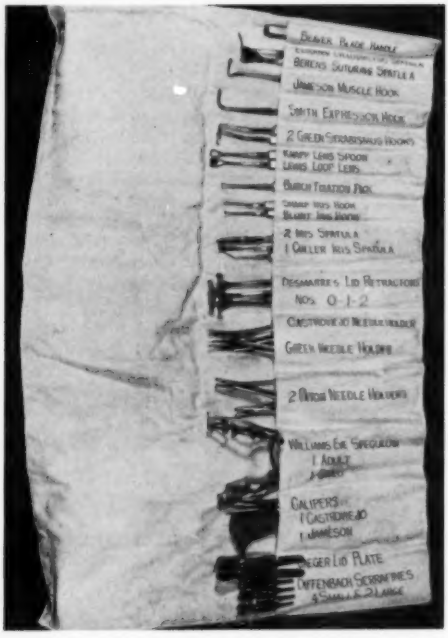

Fig. 2 (Rosenbaum). Bag containing all instruments except forceps and those for cutting.

The points of scissors are protected by short-lengths of plastic tubing. These bags, their flaps folded down to cover the exposed parts of instruments, are rolled inside out, thus avoiding contact or friction between instruments.

Sterilization

When the operating room is readied, the three bags are placed in the flash autoclave. The plastic tips are first removed from the scissors and the bags are unrolled as they are placed in the sterilizer. The knives, secured in metal racks, are also placed in the autoclave. It is true that many more instruments are sterilized than are needed but because they are spotlessly clean (as will be later described) and protected in their slots, they are not subject to undue corrosion or wear.

After removal from the sterilizer, the bags are placed on the back table and unrolled. Only those instruments scheduled to be used for the operation are picked from their slots. After the operation has begun, should the

Fig. 3 (Rosenbaum). Third bag holds scissors.

need for other instruments arise, only the clean hands of the scrub nurse may withdraw them. In this manner, unused instruments are immediately available, their location in the bags is known, they remain clean and require no postoperative handling. Unused instruments remain in the bag, clean and ready for reautoclaving without further handling.

Cleanup

Preparation for the next case, regardless of when it occurs, should begin at the conclusion of an operation. The instruments which were removed from the bags are washed in a definite routine which assures almost chemical cleanliness. To do this, soft polyethylene kitchen-type mixing bowls are used for wash basins in order that an instrument, if inadvertently dropped, sustains less damage than if dropped into a steel or enamelware container.

Detergents rather than soaps are used for cleaning instruments. Detergents in concentrations ordinarily recommended for dishwashing will produce lower surface tension and complete solution or removal of all organic tissue which ordinarily collects on instruments in use. By this method one minimizes precipitation of mineral salts with drying, as is commonly seen after washing with soap and water.

To accomplish this procedure, two polyethylene bowls are placed in the sink basin. Into the first bowl a detergent* solution is placed. The second bowl is so placed that a strong stream of water enters from the tap and overflows. Immediately after the conclusion of the operation, the tray of used instruments is brought to the sink. One at a time, the cutting instruments are swished through the detergent solution. Gentle sponging may be resorted to but is rarely necessary to remove clotted debris. The instruments are then rinsed in the second bowl receiving the running tap water and are then placed on a dry towel for momentary draining while the remaining instruments are put through the same process.

After the "sharps" and most delicate forceps are so handled, the less delicate instruments, such as needle holders, utility forceps, hooks, and so forth, are run through the same process except that three or four of them are handled at one time. All the instruments are put through this process before the next step which consists of a final rinse.

The final rinse is carried out in a third bowl containing at least a liter of distilled water. The drained instruments undergo their second rinsing by being dipped. They are handled one at a time, as before. If the instruments are to be reused immediately, they are placed on a towel-covered tray and promptly placed in the flash autoclave to be ready for use within minutes. If they are to be stored, they are transferred from the distilled water to a fresh towel to air-dry. These instruments should never be wiped dry. They drain and air-dry quickly and even if still moist when returned to their protective bags, show no stain or corrosion after drying.

Knives

At this hospital a disposable keratome blade* is used. This is made of carbon steel not stainless steel and is, therefore, handled somewhat differently. The blade is removed from its metal carrier and wiped free of oil with an ether-soaked applicator. It is then run through the detergent washing process, wiped dry, returned to its metal carrier and sterilized with the other instruments. The minimum corrosion which this method of sterilization may produce does not affect its surgical usefulness. By use of a moist sponge such spots are easily wiped from the blade immediately before use.

Inasmuch as these blades are then reserved for animal surgery by the residents, they are put through the same washing process, wiped dry, and then treated by immersion in a protective solution consisting of an ounce of

* Hemosol is used in this hospital.

* Beaver Blade.

ether to which one drop of mineral oil has been added. If so desired, this same solution may be applied to the joint of scissors when dry.

Instruments not rinsed in distilled water after washing must, of necessity, gather some mineral salts at points which cannot be reached by the drying towel. These salts will ultimately corrode even the finest stainless steel. Proof of cleanliness lies in the absence of water stains on instruments.

The use of a cloth for drying is unnecessary if the instruments are thoroughly cleaned and if distilled water is used for a final rinse. Vigorous drying with a towel may well be more abusive to instruments than their use at the actual operation.

Summary and Comment

A modified procedure for the handling, storing, cleaning, and sterilizing of instruments for surgery of the eye is presented. The advantages are the following: (1) a reduction of time required for the adequate sterilization of instruments; (2) the need for sterilizing solution for "sharps" is eliminated, thus avoiding the possibility of the inadvertent introduction of such chemicals into ocular tissues; (3) a uniform, simple method of cleaning and storing of instruments which can be followed by less experienced operating room personnel; (4) almost immediate availability of a complete set of sterile instruments necessary for the more frequently performed eye operations; (5) the protection from excess handling, resulting in less need for repair and replacement of instruments.

Department of Ophthalmology (61).

STEROID TREATMENT OF ALLOXAN-INDUCED CORNEAL OPACIFICATION AND VASCULARIZATION*

Georgia A. McCoy, B.A., and Irving H. Leopold, M.D.
Philadelphia, Pennsylvania

Since the advent of cortisone therapy, investigators have attempted to synthesize steroids with greater anti-inflammatory properties and less mineralocorticoid activity. By introducing a double bond between carbon atoms 1 and 2 of hydrocortisone the anti-inflammatory properties of steroids were increased. Three new analogues of hydrocortisone, Medrol (Upjohn), Kenacort (Squibb), Decadron (Merck, Sharp, and Dohme), have recently become commercially available. In an effort to compare these newer steroids against a standard ocular lesion, their effect on alloxan-induced corneal opacification and vascularization has been investigated.

Medrol or 6α-methyl-Δ^1-hydrocortisone is slightly soluble in water but can be dissolved in various organic solvents such as acetone, ethanol, ethyl acetate and methanol. Its stability is similar to that of prednisolone.[1]

Decadron (dexamethasone or 9-alpha-fluoro, 16-alpha methylprednisolone) is a white odorless compound. It is slightly soluble in water (0.1 mg. per cc.) and melts at 240°C. to 260°C. with decomposition.[2]

Bernstein, et al., synthesized Kenacort (triamcinolone) in 1956 by introducing a 16-alpha hydroxyl group into 9-alpha fluoroprednisolone.[3] In 1957, Thoma and his coworkers developed an economical method of synthesis by utilizing Streptomyces roseochromogenus for the introduction of the 16-alpha hydroxyl group by a fermentation procedure.[4] Kenacort, a white odorless compound, is slightly soluble in water.

Experimental Data

After removing 0.1 cc. of aqueous humor from 17, four-pound albino rabbits, an equal

* From the Research Department of the Wills Eye Hospital.

amount of 0.3 M alloxan was injected into the anterior chambers of all eyes.[5,6] Thrice daily treatment consisting of two drops of one-percent steroid administered topically was begun 24 hours later and continued daily. One group of five rabbits served as controls; three other groups of four rabbits each were treated with Kenacort, Medrol, and Decadron, respectively. All eyes were examined daily and drawings of all the corneas were made on the second, seventh, ninth, and 11th days (fig. 1). The animals were killed on the 17th day after alloxan injection.

Results

Figure 1 diagrammatically compares the degree of vascularization and edema in all eyes.

Corneal edema

By the seventh day after alloxan injection, corneal staphylomas were evident in six out of 10 of the control eyes; in four of eight Kenacort-treated eyes; in three Medrol-treated eyes; and in seven Decadron-treated eyes.

Slight swelling occurred in three control eyes; one Kenacort eye; and one Medrol eye.

At this time there was no evidence of corneal edema in one control eye; three eyes treated with Kenacort; four eyes treated with Medrol; and one eye treated with Decadron.

Nine days after alloxan injection descemetoceles had formed in one Kenacort-treated eye; two Medrol eyes; and one Decadron eye. Two days later descemetocele formation occurred in one control eye.

Corneal opacification

On the second day after introduction of alloxan into the anterior chamber, all but three eyes (two controls and one to be treated with Medrol) showed some degree of corneal opacification.

One week later there was slight improvement in two control eyes; no change in three eyes and five eyes revealed increased density. Opacification in three eyes for which Kenacort was the therapeutic agent increased;

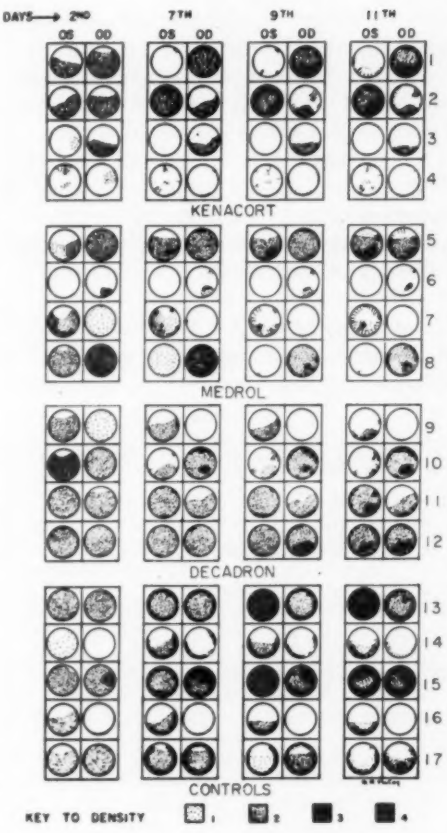

Fig. 1 (McCoy and Leopold). Corneal opacification and vascularization following injection of 0.3 M alloxan into the anterior chamber.

four eyes improved; and there was no change in one eye. Five eyes treated with Medrol improved and one showed greater opacification. There was no change in two eyes. Of the eyes treated with Decadron, there were four improvements, two increases in opacification and two eyes in which no change was evident.

There was slight to no further improvement or change in degree or extent of opacification in all eyes by the 11th day after alloxan injection.

Vascularization

On the second day after alloxan injection, one eye to be treated with Kenacort and two

eyes to be treated with Medrol showed a slight degree of vascularization.

By the seventh day all opaque eyes except one treated with Medrol and one treated with Decadron had some ingrowth of vessels.

On the ninth day vessel length increased slightly in all of the control eyes and all Kenacort-treated eyes. Slight increase in vascularization was also noted in three eyes treated with Medrol and in six treated with Decadron.

Length and density of vascularization was more marked in the control eyes on the 11th experimental day.

SUMMARY

Topically administered one-percent suspensions of Kenacort (triamcinolone), and Medrol (6α-methyl-Δ¹-hydrocortisone), appear to reduce corneal edema to a slight degree. Decadron (dexamethasone) does not seem as effective in this respect as are the preceding steroids.

These steroids all appeared to reduce corneal opacification with equal ability.

The three steroids investigated seem to retard the extent and density of corneal vascularization to a slight degree. Decadron appeared to inhibit vessel extension to the greatest degree with Medrol and Kenacort about equal in ability in this respect.

1601 Spring Garden Street (30).

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MEGALOCORNEA*

AND ITS RELATION TO CONGENITAL GLAUCOMA

ENRIQUE MALBRAN, M.D., AND RICARDO DODDS, M.D.
Buenos Aires, Argentina

According to Duke-Elder,[1] megalocornea (keratoglobus, keratomegalia, cornea globosa, megalophthalmos, and so forth) is "a bilateral developmental anomaly wherein, in the absence of a raised intraocular pressure, the anterior segment of the eye is larger than normal."

Although abnormality is more obvious in the size of the cornea, structural changes are not circumscribed to this part of the eye only; as a rule they also affect other tissues, such as the lens and the zonule, thus allowing for the designation of "gigantophthalmos," proposed by Seefelder in 1914,[1] and "megalophthalmos," proposed by Vail in 1931.[1]

On the other hand, Duke-Elder[1] defines buphthalmos (hydrophthalmos) as "a condition wherein structural abnormalities in the region of the angle of the anterior chamber offer an obstruction in the drainage-mechanism of the intraocular fluids so that the pressure of the eye is raised and a condition of congenital glaucoma results." The outstanding clinical characteristic of this ab-

* From the Italian Hospital of Buenos Aires, Ophthalmology Section. Head physician; Dr. Jorge Malbran.

normality—the author adds[1]—is the increase in the size of the entire eyeball, due to distension of the walls of the eye because of the heightened pressure.

Duke-Elder[1] makes a distinction between megalocornea and buphthalmos on the basis of nine well-known points: Descemet's membrane, degree of the corneal convexity and astigmatism, angle malformations, cupped disc, symmetry, sex frequency, heredity, and functional disorders.

This distinction between megalocornea and buphthalmos, or congenital glaucoma, as understood by Duke-Elder, is but another view of the dualist theory according to which these two diseases have been considered separate clinical entities from the time of Muralt, in 1869;[1,2] Kayser, in 1941;[1-5] Seefelder, 1914;[1-3] Haab, 1914;[1,2] Vail, 1931,[1-4] and others.

In opposition to the dualist theory, Adadie, Axenfeld, Fuchs, Von Hofe, Elschnig, De Wecker, Landolt[1,2,4,6,7] maintain that the two clinical entities in question are closely related and consider megalocornea an abortive form of congenital glaucoma.

According to Kluyskens,[7] in his complete study on the disease, three essential and pathognomonic signs point to the diagnosis of congenital glaucoma:

1. The increase in diameter of the cornea, which must exceed 12 mm., together with increase in the volume of the eye.
2. Unusual depth of the anterior chamber.
3. Abnormal persistence of mesodermal tissue at the angle of the anterior chamber.

The following three symptoms he terms *secondary:*

1. Presence of ruptures in Descemet's membrane.
2. Opacities in the corneal parenchyma.
3. Hypoplasia of the iris stroma.

Kluyskens considers that ocular hypertension is but an added symptom of exceptional gravity and that from the clinical point of view it will reflect in an acute stage corneal edema and secondary atrophy with cupping of the optic nerve, if the intraocular pressure is not normalized.

In Kluyskens's[7] opinion, when the three pathognomonic signs concur without hypertension, the syndrome must be considered incomplete congenital glaucoma.

When ocular hypertension is added to the three essential signs, appearing in the first weeks of life, it is a case of complete early congenital glaucoma; when it appears several years later, then it is a case of complete late congenital glaucoma.

In their essay on congenital glaucoma—which they prefer to call hydrophthalmos—Gallenga and Matteucci[4] distinguish three clinical varieties:

1. *Pure hydrophthalmos,* with increase in the diameter of the cornea, abnormalities at the angle level, deep anterior chamber, increase in size of lens, absence of ocular hypertension and a relatively mild clinical evolution.

2. *Complicated hydrophthalmos,* with hypertension and inflammatory processes, anterior chamber also deep, serious evolution and marked functional disorders.

3. *Malignant early hydrophthalmos,* showing a reduced or abolished anterior chamber and warranting extremely bad prognosis, not only as to vision but also as to preservation of the eyeball.

Kluyskens's[7,8] incomplete congenital glaucoma, also interpreted as such by L. and R. Weekers,[9,10] and by François,[3] corresponds to Gallenga and Matteucci's pure hydrophthalmos, an entity characterized by abnormal dimensions of the cornea, deep anterior chamber, persistence of mesodermal tissue at the angle and absence of hypertension. In Kluyskens's opinion, the majority of the clinical attributes characteristic of megalocornea and which are the cornerstone of the dualist theory, are not exclusive to this disease, having been observed by him in what he terms incomplete congenital glaucoma. This author considers that there are only two arguments to justify the existence of a proper megalocornea:

1. Kayser's anatomicopathologic examina-

tion, which has proved in a case of megalocornea that the angle was normal, Schlemm's canal well developed and correctly situated, and where the dimensions of the posterior segment of the eye were also normal.

2. The existence of families afflicted by megalocornea, where glaucomatous symptoms have never been known to appear (Kayser and Gronholm's genealogic trees).

Gallenga and Matteucci[4] do not consider that there is sufficient clinical data to admit the existence of pure megalocornea and continue accepting the dualist theory. These authors are of the opinion that Kayser's case, already mentioned, was a typical keratoglobus (megalocornea globosa), in view of the curvature of the cornea, the iridocorneal angle, the anterior chamber, position of the iris, and so forth, all of these characteristics absolutely different to those encountered in hydrophthalmos and megalocornea. They deem that Kayser's merit lies in having described, anatomically, a keratoglobus, although the designation he applied to his case (megalocornea globosa) subsequently proved equivocal when others suppressed the term globosa and so gave rise, on false grounds, to the dualist theory.

Gallenga and Matteucci maintain the unitary theory and consider megalocornea an initial, self-limited or cured form of hydrophthalmos, a view to which they attribute great importance for a clearer understanding of the exact nature of hydrophthalmos.

Undoubtedly, as both Kluyskens[7] and François[3] contend, thanks to gonioscopy an end can be put to the discussion between the unitary and the dualist theories. It has been possible to establish, by this method of examination, that many megalocorneas are, in fact, incomplete congenital glaucomas[3, 7–10] presenting as they do abnormal persistence of mesodermal tissue at the angle level, whence it may be asserted that pure megalocornea with no abnormalities at the iridocorneal angle exists, and that it is a mere abnormality of construction.[2, 3, 7]

In the face of these arguments, although the existence of pure megalocornea is, apparently, accepted, the diagnosis can only be applied to cases that do not present characteristic disorders upon gonioscopy.

In accepting, then, pure megalocornea as an independent entity, the dualist theory would still hold good, though it has obviously lost ground in a great number of cases which, thanks to gonioscopy, are now interpreted as incomplete forms of congenital glaucoma, and which strengthen the interpretation of both these abnormalities as one.

The finding, in members of the same family, of megalocornea without hypertension and typical buphthalmos (complete congenital glaucoma), as observed by Falls,[3, 10] L. and R. Weekers[9] and ourselves (Cases 1, 2, and 3), would appear to support the existence of a close connection between these diseases, as the followers of the unitary theory maintain. To corroborate this position, François[3] mentions having examined a patient with typical buphthalmos in one eye, and megalocornea without hypertension in the other.

The association of megalocornea and congenital glaucoma with other morbid entities which we will consider further on, is another point in support of the close identity of these syndromes. The way both diseases are inherited, which was another of the outstanding points favoring the differential diagnosis, has also lost ground as an argument for distinction.

Nor is it an absolute fact that megalocornea is, as it was considered, the exclusive patrimony of the male sex in 92 percent of cases—which would appear to reflect recessive sex-linked inheritance in which women were the carriers—for various forms of inheritance have been observed in different genealogic trees (Horner-Bollinger type, predominantly Mendelian type, and so forth) (Kluyskens[7]). Furthermore, there are many examples of megalocornea in women (Cases 1, 2, 3, 4, 7, and 8 in our data) and which do not correspond to consanguinity in the parents, according to Gron-

holm. The greater frequency in the male sex is also characteristic of congenital glaucoma: 5/3, Duke-Elder;[1] Kluyskens,[7] of 31 patients 26 were of the male sex—in other words, two thirds of the cases, which is in keeping with most statistics; Grosz (1932) 62 percent, Zahn (1904) 58.9 percent, Kunzmann (1899) 70 percent.

The family character of buphthalmos has been the subject of many publications confirming this peculiarity; but as for the hereditary factor of the disease, the manner in which it is inherited has not been finally cleared, the respective literature only covering two affected generations.

The majority of cases are explained through recessive inheritance, according to Delmarcelle[11] on: (a) the presence of consaguinity in seven percent of cases; (b) the fact that the parents of buphthalmic patients are phenotypically normal; (c) the possibility of a buphthalmic patient producing normal descendants; (d) the recessivity of the disease in rabbits (Vogt 1919, Franceschetti, 1930).

Twenty-three genealogic trees so far published with buphthalmos in two successive generations do not provide sufficient grounds, in the opinion of Delmarcelle[11] to doubt the recessive quality of the transmission in favor of a dominant inheritance; this would require a greater number of examples than current literature has to offer at present.

Hence, the manner of inheritance varies both in megalocornea as in congenital glaucoma, and we are inclined to agree with Kluyskens[7] that it will be necessary to wait until certain facts prove beyond a doubt that congenital glaucoma and certain forms of megalocornea are one and the same disease, in order that the theories on the respective transmission may be definitely established.

Alterations of angle on gonioscopic examination

We have stated so far that, in the opinion of various authors, gonioscopy is the only procedure whereby pure megalocornea may be differentiated from incomplete congenital glaucoma inasmuch as gonioscopic examination allows for the absence of anatomic anomalies in the former case, and presence of some in the latter, to be established.

According to Kluyskens,[7] the anomalies most characteristic of congenital glaucoma, visible on gonioscopy, are: persistence of mesodermal tissue, abnormal aperture of the angle and almost constant absence of Schlemm's canal. Upon close observation of the different alterations found in the various elements, we can say with Kluyskens:[7]

a. *Iris root.* Around the periphery shows a marked thinning of the anterior layer, together with atrophy in more or less extended plaques. The ciliary border is rarely visible, and only the presence of circular vascular loops makes it possible, sometimes, to identify the boundary of the iris root.

b. *Ciliary body.* Since the angle is abnormally wide, the same occurs with the ciliary band. It is, however, exceptionally visible in congenital glaucoma, being generally covered by a mesodermal tissue varying in color from light yellow to dark brown. There are some cases where anomalies are less coarse, in which the ciliary band is visible through a mesh of abnormally developed iridian trabeculae (our Cases 2, 3, 4, 7, 10, 11, 13, and 15).

c. *The iridian trabeculae* (Troncoso's rudimentary pectinate fibers) appear abnormally developed, in the form of an embryonic tissue that lines the bottom of the angle, and in which two more current aspects are distinguishable, depending on the contrast between the color of the iris and of the actual trabeculae. When the iris is blue or shows scant pigmentation, then the mesodermal tissue is generally a more or less dense light yellow, and extends to the base of the iris; in these cases the division between the iris and trabeculae is fairly clear. When the iris is darker, the iridian trabecula (mesodermal tissue) is the same color or can be even darker, and extends with no

line of transition from the base of the iris (our Cases 1, 5, 6, 8, and 9). The latter variety is inclined to give the impression that the base of the iris is inserted higher up than is normal, at the level of the scleral trabeculae, or even of Schwalbe's ring. This has led several authors to construe the anomaly in question as a high insertion of the iris (Troncoso, Sugar, Barkan, mentioned by Kluyskens[7]) when it is, in point of fact, a case of a tissue situated beyond the iris root —itself normally placed—and which is usually distinguishable from the latter by the presence of the circular vascular loops. In other instances the iridian trabecula retains the form of numerous abnormally developed iridian processes covering the ciliary band, like filamentary goniosynechias inserted on the trabeculae at different levels.

d. *Scleral trabeculae.* The scleral trabeculum usually retains its normal aspect and, according to Kluyskens, in certain cases of incomplete glaucoma sometimes develops a dark brown, almost black hue, which can be due either to the presence, on the surface, of a highly pigmented embryonic tissue, or to a marked pigmentation of the actual trabeculae (certain cases of pigmentary glaucoma—Malbran[12]).

e. *The scleral spur* is rarely visible.

f. *Schwalbe's ring* shows no alteration peculiar to congenital glaucoma, except when the condition is accompanied by posterior embryotoxon (our Cases 10, 11, and 12).

g. *Schlemm's canal* is nearly always invisible to gonioscopy.

h. *Peripheric iridonesis.* This phenomenon has been observed by Malbran,[12] Gallenga and Matteucci,[4] Barkan,[13] and our Cases 4, 6, and 10.

The persistence of aberrant meshwork at the angle, of which we have described the main gonioscopic characteristics, has been interpreted so far as a development alteration that hinders reabsorption through atrophy of the tissue in question, intended for disappearance during life (Seefelder and Wolfrum[7, 8, 13]). However, lately Allen, Burian and Braley[14] in sundry embryologic investgations on the formation of the angle, have discarded the contention that it is formed by absorption or atrophy of mesodermal tissue in favor of a cleavage between the iris stroma and the trabecula pertaining to the uvea.

Recently Maumenee,[15] after reviewing the more widely accepted theories on congenital glaucoma pathogenesis, submits his own theory grounded on the histologic examination of over 40 eyes with congenital glaucoma. Briefly, the author states that he has been able to prove that, in many cases, the meridional fibers of the ciliary body insert into the trabecula in front of the scleral spur. On contraction, these anteriorly inserted fibers are capable of collapsing Schlemm's canal, and thus blocking the outflow of aqueous.

Other syndromes with anatomic anomalies at the level of the iridocorneal angle

Persistence of an abnormal tissue at the angle level established by gonioscopy is not exclusive to congenital glaucoma in its different clinical varieties; this has also been observed in a number of other diseases, some of them related to congenital glaucoma and others interpreted as entirely independent diseases in which ocular hypertension also is not an obligatory symptom.

Juvenile glaucoma and *congenital glaucoma* are considered by Gross, Loehlein, Waardenburg, Ellis (Kluyskens[7]) to be diseases of identical origin, differing only in the power of distension of the eye wall. The observation by Stokes (L. and R. Weekers[9]), who relates sundry examples of brothers and sisters affected some by juvenile glaucoma and others by congenital glaucoma, is a highly suggestive example of this interpretation.

We, however, agree with François, Deewer and Van Den Berghe,[6] whose opinion is likewise shared by Weekers and Watillon,[16] that the designation of juvenile glaucoma must be abandoned in order to avoid

confusion, since the term includes: open-angle glaucomas appearing at an early stage and often presenting a hereditary character; certain typical congestive glaucomas caused by mechanical blocking in narrow angles; and, finally, also congenital glaucoma of late onset, with persistence of mesodermal tissure at angle level.

This third variety of the ailment, heretofore termed juvenile glaucoma, is the only manifestation which can actually be identified with congenital glaucoma and which constitutes a typical expression of Kluyskens's complete late congenital glaucoma. These cases can have evolved up to the onset of hypertension as simple megalocorneas (our Cases 1, 14, and 15; Kluyskens's Case 2); or have evolved without alteration in the corneal diameters, as in the cases of Weekers and Wattillon,[16] François[17] and our Cases 9 and 12.

Gallenga and Matteucci,[4] despite the observation by Stokes already mentioned and the anomalies of the iridocorneal angle found in certain cases of juvenile glaucoma (Weekers and Wattillon,[16] Kluyskens,[8] François,[6,17] Allen and Ackermann,[20]) do not consider these of sufficient value to justify the connection between juvenile glaucoma and hydrophthalmos, maintaining as they do that hydrophthalmos is a typical malformation of the eye which is present at birth, and is characterized mainly by the abnormal enlargment of the eyeball, especially of the cornea, while this clinical attribute is not always to be observed in juvenile glaucoma.

Recently, and based on certain gonioscopic characteristics, J. Malbran[12] has drawn attention to the close relationship that can exist between pigmentary glaucoma and congenital glaucoma; it will be observed that the cases he cites include juvenile glaucoma, glaucoma appearing in adults, megalocornea without hypertension, the former being nothing else than late congenital glaucoma and the latter incomplete congenital glaucoma, if Kluyskens's contention is to be adopted.

In cases of progressive myopia, where the ophthalmotone is not altered nor the corneal diameters increased sufficiently to warrant a diagnosis of megalocornea, we have found, on gonioscopic examination, many of the congenital anomalies already described; this discovery has drawn our attention considerably, and we insert it at this stage merely as a curiosity, although for the time being we have not attempted to draw any conclusions. We will add, however, in this regard, that we have had occasion to examine the mother of a typical buphthalmos patient, who suffered from progressive myopia, with ophthalmotone unaltered and normal corneal diameters, and who, on gonioscopy presented a wide angle with a tissue differing from that of the iris, of a jellyish consistency, covering the ciliary band, and the iris root perfectly delineated by a great number of tortuous circular vascular loops.

In aniridia, in Marfan's syndrome, in pupillary ectopia, in microcornea, polycoria, cornea plana, and so forth, it is equally current to prove anatomic anomalies at the iridocorneal angle level.

In Rieger's "disgenesis mesodermalis iridis e corneae," which comprises Axenfeld's posterior embryotoxon or Streiff's[4,10] posterior marginal dysplasia, v. Hippel's[4,5] syndrome (congenital anomaly characterized by the adherence of a corneal opacity to the iris tissue), angle anomalies are also often present, as warranted by repeated gonioscopic observations.[4,19,20]

The observation in the same family by L. and R. Weekers[9] of megalocornea, embryotoxon, anomalies of the iridocorneal angle and of the iridian structure, pupil ectopia, alterations in the shape of the pupil, buphthalmos (the latter in association with a typical Marfan syndrome); and also the finding by Falls (Weekers, L. and R.,[9]) of microcornea or megalocornea, embryotoxon, anomaly in the shape and position of the pupil, polycoria, ectropion uveae, buphthalmos in the same family, has led this latter author to believe in the existence of a gene producing sundry malformations in the an-

terior segment. L. and R. Weekers[9] stress that the observation of these families points to the importance of the different mesodermal malformations in the genesis of congenital glaucoma. Gallenga and Matteucci[4] consider that all these congenital diseases of the chamber and so forth should be grouped within the wide picture of "congenital dysplasia of the iridocorneal angle," which is intimately connected with the developmental process of the sclerocorneal limbus.

Relation between angle anomalies, ocular hypertension, and congenital glaucoma

The finding of an abnormal tissue filling the iridocorneal angle together with ocular hypertension would seem to point to the hypertension being due to an obstruction in the fluid discharge from the anterior chamber caused by the presence of the abnormal tissue. This most alluring interpretation is confirmed, apparently, in certain cases of hypertension with anomalies of the angle, in which the tonography reveals a reduced outflow coefficient and where the faulty discharge is answerable for the increase in ocular tone. Although a reduction in outflow has been established in nearly all the cases of complete congenital glaucoma we have had occasion to examine and we agree on this point with Weekers and Wattillon,[16] this does not imply that the site of the obstruction lies in the angle, a fact which has been stressed by several authors, among them recently Maumenee.[21] On the other hand, as L. and R. Weekers[9] have proved the presence of angle anomalies in diseases which are not accompanied by ocular hypertension and which coexist with typical buphthalmos in the one family, it is impossible, for the present, to attribute to the iridocorneal malformations the fundamental pathogenic role in the genesis of hypertension.

Neither has the study of Ascher and Goldmann's aqueous veins thrown light on the interpretation of tension alterations in hydrophthalmos (L. and R. Weekers,[9] Gallenga and Matteucci[4]).

L. and R. Weekers[9] are inclined to believe the hypertension due to vascular anomalies in the uvea, anomalies which are often proved histologically and which would appear to bring about not only a modification in aqueous discharge, but also, principally, an alteration in the exchange of water that takes place at capillary level, thus disrupting the entire movement of water.

J. Malbran[12] is not of the opinion, either, that the mechanical cause present in congenital glaucoma at the level of the chamber angle is sufficient to warrant the variations in pressure. Furthermore, this author adds, in many megalocorneas with the same angle alterations, the intraocular pressure is not affected (our Cases 2, 3, 4, 5, 6, 7, 8, 10, and 13).

We maintain, with J. Malbran[12] that is must be inferred that such anatomic anomalies reflect a more or less significant morphologic alteration in the eyes affected, where they are placed in a situation of inferiority in the face of any agent capable of bringing about a neurotension disturbance. And with regard to this latter point, we must add with Gallenga and Matteucci[4] that it is not unusual to observe in children the transformation of a case of pure hydrophthalmos to complicated hydrophthalmos, with congestive and hypertension symptoms resulting from a toxic infectious disease.

Different degrees of anatomic anomalies at the iridocorneal level would appear to point, clinically, according to the respective importance, to a more or less serious evolution in given cases. This contention is proved in the cases reported by Kalt, Dubois Poulsen (Kluyskens[7]), and in our Cases 1, 2, and 3.

Krowels (Klyuskens[7]), when studying six patients with unilateral typical buphthalmos, found that the unaffected eyes showed anomalies of different degrees, though less marked than in the buphthalmic eye; these anomalies would allow for satisfactory preservation of the functional condition of the eyes in question, and impressed Krowles as stages of transition. Kluyskens,[7] in com-

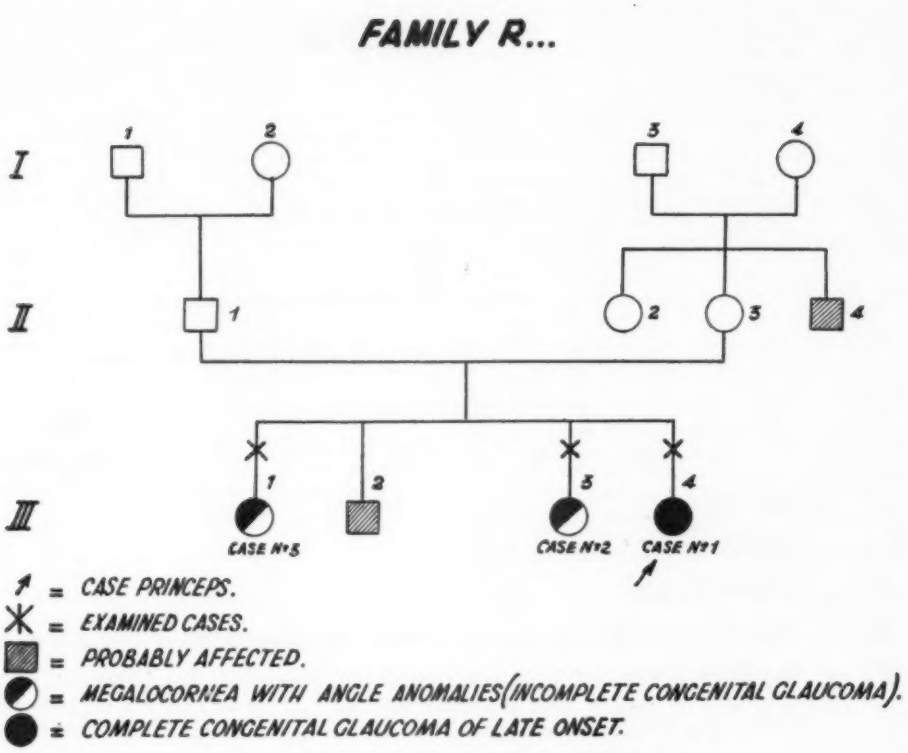

Fig. 1 (Malbran and Dodds). Illustrating cases in Family R.

menting on the above, states that "the varying degree of persistence of embrionary tissue which is reflected in multiple and ever different aspects of the angle, deserves to be considered since, according to its importance, it can represent an index of seriousness in congenital glaucoma." We consider we have contributed toward this view with our findings in the R . . . family, the first three cases listed herein (fig. 1). The only one of the three sisters with megalocornea to develop complete congenital glaucoma, with the serious evolution commented upon, presented, on gonioscopy, a marked alteration (Case 1); while the other two sisters, with megalocornea and functionally healthy eyes, no doubt had remains of mesodermal tissue at the angle, though to a decidedly lesser degree (Cases 2 and 3). Furthermore, we can state that, in the majority of cases of complete and early congenital glaucoma (complicated hydrophthalmos), we have found marked anomalies of the angle comparable to Case 1; while in the cases of incomplete congenital glaucoma (pure hydrophthalmos) or where hypertension set in at a later stage, the modification at the angle level, though obvious, was less marked.

Case reports

Case 1

Elsa R., 19 years of age.

History. Abnormal size of both eyes from birth. Patient was treated during school age, as a myope. At the age of 13 years, signs of ocular congestion and progressive reduction of vision. Congenital glaucoma was diagnosed, and the patient was operated repeatedly, without achieving final normalization of the intraocular pressure.

Family history. Two sisters (Cases 2 and 3) with megalocornea; one brother and one uncle on the mother's side had a similar appearance of the eyes.

Both eyes presented a 16-mm. corneal diameter. No ruptures in Descemet's membrane. Deep anterior chamber. Miotic pupils. Pupillary membrane. R.E., 10/300; L.E., hand movements. Intraocular

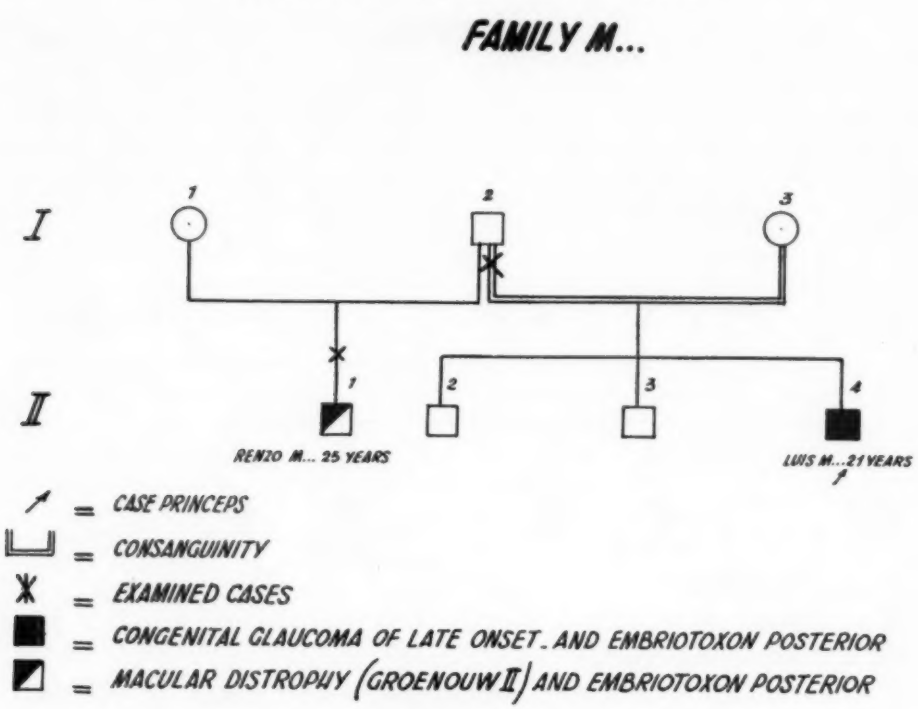

Fig. 2 (Malbran and Dodds). Illustrating cases in Family M.

pressure: R.E., 45 mm. Hg; L.E., 50 mm. Hg (Schiøtz).

Gonioscopic examination. The gonioscopic appearance is very similar in both eyes. Marked atrophy of the anterior plane of the iris. Near the angle the iris changes color, turns darker, and is inserted along a looping line just below Schwalbe's ring. This darker section of the iris radiates finger-like prolongations on its surface toward the pupillary zone. Gonioscopic appearance of high insertion of the iris.

Summary. Kluyskens's complete congenital glaucoma. Gallenga and Matteucci's complicated hydrophthalmos of late onset.

CASE 2

Leonor R., 22 years of age.

History. She does not complain of any ocular symptoms.

Family history. See Case 1.

Both eyes showed 13 mm. corneal diameter. R.E., 20/20; L.E., 20/20. Intraocular pressure: R.E., 18 mm. Hg, tonographic (C) 0.23 mm.³/min./mm. Hg; L.E., 17 mm. Hg, tonographic (C) 0.25 mm.³/min./mm. Hg (Schiøtz). Deep anterior chamber.

Gonioscopic examination. Wide angle. Hypotrophy of the anterior segment of the iris. Vascular loops at the iris root. Iridian trabeculae in considerable quantity forming a meshwork through which the ciliary band can be seen.

Summary. Familial megalocornea, with structural alterations of the angle. Kluyskens's incomplete congenital glaucoma.

CASE 3

Amelia R., aged 29 years.

History. Patient wears astigmatic correction.

Family history. See Case 1.

Both eyes presented 12-mm. corneal diameter. R.E., 20/30, with a +0.75D. cyl. ax. 105°; L.E., 20/40, with a +1.0D. cyl. ax. 100°. Intraocular pressure: R.E., 20 mm. Hg, tonographic (C) 0.20 mm.³/min./mm. Hg; L.E., 18 mm. Hg, tonographic (C) 0.22 mm.³/min./mm. Hg (Schiøtz). Deep anterior chamber.

Gonioscopic examination. Very similar to her sister's (Case 2).

Summary. Familial megalocornea with structural alterations of the angle. Kluyskens's incomplete congenital glaucoma.

CASE 4

Celia B., 53 years of age.

History. From the age of nine years she has worn glasses for her myopia and recently has noted

a gradual reduction in her sight. No family history.

The corneal diameter was 15 mm. in both eyes. Visual acuity was 20/100 in both eyes. Both lenses had undergone nuclear cataracts and were subluxated. Intraocular pressure: R.E., 20 mm. Hg (Schiøtz); L.E., 21 mm. Hg. Deep anterior chamber. Marked hypoplasia of the iris stroma, especially on the inferior segment. Notch coloboma and hyperplasia of the pigment border (flocculi). Iridonesis.

Gonioscopic examination. Very wide angle ("arrondi"). Circular vascular loops on the iris root. The ciliary band is covered by a tissue of the same appearance as the iris, but darker and vertically disposed. The scleral spur, the trabecullar meshwork and Schwalbe's ring are normal. The left eye had a round-pupil intracapsular cataract extraction with a peripheral iridectomy. The actual visual acuity on the operated side is 20/50 with a −1.5D. sph. ⊃ −1.25D. cyl. ax. 35°. Intraocular pressure: L.E., 16 mm. Hg (Schiøtz).

Summary. Megalocornea with marked anomaly at the angle. Nuclear cataract and subluxated lens. Kluyskens's incomplete congenital glaucoma.

CASE 5

Ernesto Z., 28 years of age.

History. Myopia from the age of seven years. Gradual reduction of eyesight. The right eye had undergone a cataract extraction by another surgeon, with unsatisfactory results. Corneal diameter, 12 mm. on both sides. The left eye presented a very deep anterior chamber, hypoplasia of the iris stroma, iridonesis, subluxated lens and total cataract. The right eye did not have light perception, the left eye only hand movements. Intraocular pressure: R.E., completely hypotonic; L.E., 16 mm. Hg (Schiøtz).

Gonioscopic examination. Wide angle. Iridian trabeculae in considerable quantity covering the ciliary band ending at different levels on the spur and scleral trabeculae.

Summary. Megalocornea. Angle anomaly. Subluxated total cataract.

CASE 6

Alfredo P., 50 years of age.

History. Poor vision from childhood. Recently lost the sight of his right eye.

Family history. Patient relates that one of his sons suffers from something similar in his eyes. Unfortunately we were not able to examine him.

Corneal diameter, 14 mm. on both sides. The right eye only had light perception. The left eye, 20/200. Intraocular pressure: Both eyes, 18 mm. Hg (Schiøtz). Deep anterior chamber. The right lens had undergone total cataract, and the left eye a posterior cortical opacity. Marked hypoplasia of both iris stroma.

Gonioscopic examination. Very wide angle ("arrondi"). Vascular loops at the iris root in considerable quantity. Peripheral iridonesis. Very thick

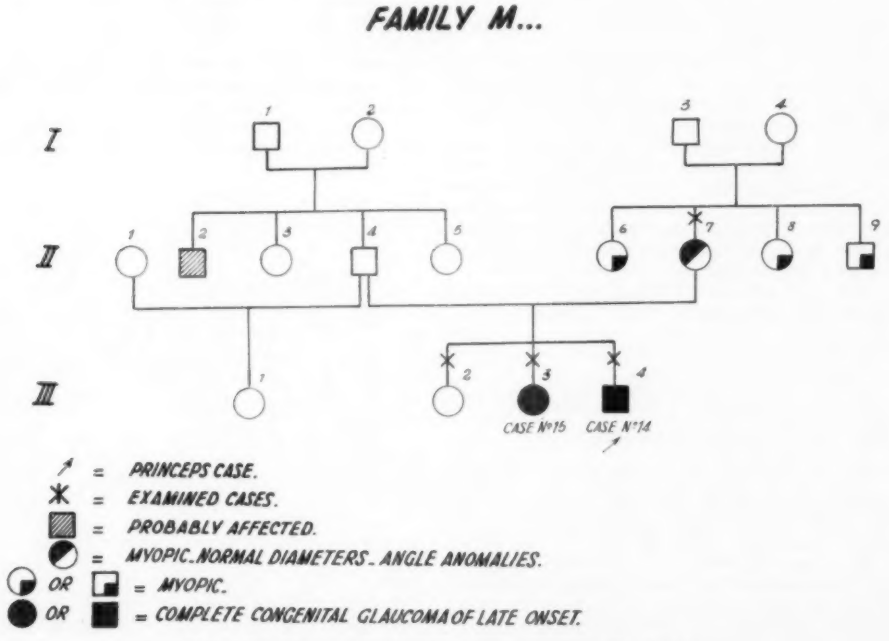

Fig. 3 (Malbran and Dodds). Illustrating cases in Family M.

iridian trabecula, yellow in color, clearly distinguishable from the iris, from which radiate prolongations.

Summary. Megalocornea with marked alterations of the angle. Cataractous lenses. Kluyskens's incomplete congenital glaucoma.

CASE 7

Graciela F., six years of age.

History. Bone formation and height pertaining to eight years of age. Estrogen sediment in urine; abnormal development of mammary glands; increase in the pituitary fossa; prognathism. Probable precocious puberty. No family history.

The corneal diameter was 13 mm. on both sides. Visual acuity: R.E., 20/50; L.E., 20/40. Intraocular pressure: R.E., 16 mm. Hg (Schiøtz); L.E., 17 mm. Hg. Deep anterior chamber.

Gonioscopic examination. Very wide angle. Hypoplasia of the anterior layers of the iris. Some vascular loops at the iris root. In both eyes, some iridian trabeculae, which give the impression of being filamentary goniosynechias that insert below the scleral spur and through which the ciliary band is seen.

Summary. Megalocornea. Alterations of the anterior chamber angle in a girl in whom puberty will probably be precocious. Kluyskens incomplete congential glaucoma.

CASE 8

Esther V., 13 years of age.

History. The parents consulted because of the abnormal appearance of both eyes.

No family history.

The corneal diameter was 13 mm. in the right eye, and 12.5 in the left eye. Visual acuity was 20/20 in both eyes. Intracular pressure: R.E., 15 mm. Hg, tonographic (C) 0.25 $mm.^3$/min./mm. Hg; L.E., 16 mm. Hg, tonographic (C) 0.28 $mm.^3$/min./mm. Hg (Schiøtz). Deep anterior chamber.

Gonioscopic examination. Wide angle. The entire ciliary band sector is covered by a dark brown tissue, different from the iris stroma. Some filaments of this tissue join the iris root with the inferior border of the scleral spur.

Summary. Megalocornea with angle alterations. Kluyskens's incomplete congenital glaucoma.

CASE 9

Oscar R., seven years of age.

History. During the past year, his parents had noticed a marked diminution of his sight, with a concomitant congestion of his eyes.

No family history.

The corneal diameter with 11 mm. on both corneas. Visual acuity was 20/80 for the right eye, and 20/60 for the left. Intraocular pressure (under general anesthesia): R.E., 32 mm. Hg (Schiøtz); L.E., 37 mm. Hg. Both corneas presented a marked edema. Dilation of the arteriovenous bundle and ectasia of some capillaries of the limbal vascular network (with the same characteristics encountered by Gallenga and Matteucci in complicated hydrophthalmos.) Both fundi presented a fine scattered pigmentation that was particularly numerous at the periphery.

Gonioscopic examination. Examination was undertaken after one drop of glycerine (to reduce corneal edema). Deep anterior chamber. The angle resembled the known appearance of anterior insertion of the iris, where the scleral spur and ciliary band were not visible.

Summary. Kluyskens's complete congential glaucoma, or Gallenga and Matteucci's complicated hydrophthalmos, of late onset.

CASE 10

José F. L., 47 years of age.

History. On his first visit he complained of a sudden loss of vision on the left side two months ago. Three years before the same eye had undergone a cataract extraction. There was no visual discomfort in the right eye.

No family history.

Both corneal diameters were 13 mm. Visual acuity was 20/25 in the right eye (without correction) and in the left there was light perception. The left eye presented total retinal detachment with marked fixed folds. The right eye had a remarkably deep chamber. Intraocular pressure: R.E., 18 mm. Hg (Schiøtz); L.E., 10 mm. Hg.

Gonioscopic examination. Wide angle ("arrondi"). Peripheral iridonesis. A wide ciliary band was partially covered by a tissue of the same color as the iris. About eight to 10 iridian trabeculae were observed on each field examination. The scleral spur was partially invisible. Posterior embryotoxon, where some iridian trabeculae were inserted. The patient refused any operation on the left eye and the visual status of the right eye did not change during a two-year follow-up.

Summary. Megalocornea, with typical alterations of the angle. Kluyskens's incomplete congenital glaucoma.

CASE 11

Carlos C., 15 years of age.

History. Myopia from the age of seven years.

No family history.

The corneal diameter was 14 mm. on both sides. Visual acuity was: R.E., 20/100, with a —14D. sph. $\frown$ —2.0D. cyl. ax. 10°; L.E., 20/70, with a —13D. sph. $\frown$ —1.0D. cyl. ax. 170°. Intraocular pressure: R.E., 14 mm. Hg (Schiøtz); L.E., 16 mm. Hg. Mittendorf knots and a "spurious cataract" were noted on both lenses.

Gonioscopic examination. Very deep anterior chambers. The Schwalbe's ring was prominent (incipient embryotoxon). A great quantity of iridian trabeculae covered the ciliary band like a meshwork.

Summary. Megalocornea. Angle anomalies. Kluyskens's incomplete congenital glaucoma.

CASE 12

Luis M., 21 years of age.

History. Patient has been medically treated for glaucoma during the past two years.

Family history. Parents are first cousins; his two healthy sisters were not examined by us. The father was married twice, Luis being a child of the second marriage. There was only one child of the first marriage, Renzo M., who is 25 years of age, and presents a macular corneal dystrophy (Groenouw II) together with an obvious posterior embryotoxon. It is interesting to stress that in Renzo M., Schwalbe's ring was salient and covered the scleral trabeculae like a cornice, this being a typical characteristic of embryotoxon, E. Malbran[22] (fig. 2).

Both corneal diameters measured 12 mm. Visual acuity was: R.E., 20/40; L.E., 20/25. Intraocular pressure: R.E., 32 mm. Hg (Schiøtz) (scleral rigidity, 0.0190); L.E., 49 mm. Hg (Schiøtz) (scleral rigidity, 0.0190) (Friedenwald's 1955 nomogram).

Gonioscopic examination. Deep anterior chamber. Hypoplasia of the anterior layers of the iris stroma. In the right eye, an enormous iridian crest, triangular in shape, covers the ciliary band and trabecular meshwork like a bridge, inserting on the salient border of Schwalbe's ring. Vascular loops were noted at the iris root.

This patient on May 5, 1958, had a "filtering iridectomy" (J. Malbran and E. Malbran[23]) in both eyes at the same sitting. The intraocular pressure was definitely normalized on the right eye (19 mm. Hg [Schiøtz]) but in the left eye, although the intraocular pressure was markedly decreased (32 mm. Hg [Schiøtz]), a similar operation was necessary five months later, when the intraocular pressure was finally normalized (16 mm. Hg [Schiøtz]).

Summary. Congenital glaucoma of late onset. Posterior embryotoxon, normal corneal diameters. Consanguinity (recessive linkage). One step-brother also with posterior embryotoxon and a macular dystrophy (recessive linkage).

CASE 13

Jorge B., 12 years of age.

History. Patient lost his left eye six years ago, through a perforating corneal injury.

No family history.

The right corneal diameter measured 14 mm. Visual acuity was: R.E., 20/50 with a 5.5D. sph. ⊂ —0.5D. cyl. ax. 90°. Intraocular pressure: 19 mm. Hg (Schiøtz). Suture cataract.

Gonioscopic examination. Deep anterior chamber "Arrondi" angle. Schlemm's canal with blood. Abundance of iridian trabeculae covering the ciliary band and part of scleral trabecula, like a meshwork.

Summary. Incomplete congenital glaucoma. Megalocornea with angle alterations.

CASE 14

Juan M., 34 years of age.

History. The left eye, that was buphthalmic on the patient's own testimony (and according to photographs taken when he was younger, which we had occasion to examine) had suffered a retinal detachment 10 years ago. Subsequently it was enucleated. The right eye was operated for glaucoma (iridencleisis) by another surgeon, a year ago.

Family history. No consanguinity was known; however, the parents belong to families that have lived for more than 10 generations in a village of 6,000 inhabitants in the south of Italy. By heresay, a brother of the patient's father suffered from a similar condition. Three brothers of the mother are myopes. The mother is also a myope, with normal corneal diameters but presenting an "arrondi" chamber angle with marked iridian trabeculae. One of the patient's sisters (Case 15) presents congenital glaucoma of late onset (fig. 3).

The corneal diameter was 13 mm. on the right eye. Visual acuity 20/20, with a —0.25D. sph. ⊂ —1.0D. cyl. ax. 10°. The right eye presented the usual appearance of an iridencleisis, with a flat filtering scar.

In spite of being submitted to a filtering operation, the intraocular pressure was not completely normalized. At different checkings, it varied from 43 to 32 mm. Hg, in spite of medical treatment with miotics, Epitrate, and Diamox.

Gonioscopic examination. The patient showed a marked hypoplasia of the iris stroma. The anterior chamber was very deep and the angle showed broad annular goniosynechias.

Summary. Family type complete congenital glaucoma of late onset.

CASE 15

Teresa M., 36 years of age.

History. She has worn glasses for myopia from the age of eight years.

Family history. See Case 14.

The corneal diameter was 14 mm. on the right and 13 mm. on the left. Visual acuity: R.E., 20/200 with a —10D. sph.; L.E., 20/50 with a —8.0D. sph. Intraocular pressure: R.E., 43 mm. Hg (Schiøtz) (scleral rigidity, 0.0137); L.E., 27 mm. Hg (scleral rigidity, 0.0137).

Gonioscopic examination. Very deep anterior chamber. Wide angle ("arrondi"). The ciliary band was markedly pigmented. Iridian trabeculae in large quantity covering the ciliary band like a meshwork.

Summary. Kluyskens's complete congenital glaucoma of late onset, or Gallenga and Matteucci's complicated hydrophthalmos of a family type.

SUMMARY AND CONCLUSIONS

All the cases presented the three pathognomonic symptoms essential to congenital glaucoma according to Kluyskens: (1) increase in corneal diameter, which must exceed 12 mm.; (2) deep anterior chamber; (3) abnormal persistence of embryonic mesodermal tissue at the iridocorneal angle.

Case 9 (a seven-year-old boy) was the

only one to present a corneal diameter of less than 12 mm. However, this case presented other secondary signs, corneal edema and hypertension, so that the normal corneal diameter does not invalidate the diagnosis of congenital glaucoma.

Of the three secondary symptoms, out of 15 cases 10 showed a certain degree of atrophy of the iris.

Of the 15 cases, only five (1, 9, 12, 14, and 15) presented ocular hypertension as an added symptom, and they represent typical clinical forms of complete late congenital glaucoma which had evolved, up to the time hypertension set in, as simple megalocorneas.

The 10 remaining cases, in which there were different varieties and intensities of megalocornea, in view of the presence of the three pathognomonic signs of congenital glaucoma and the absence of the added symptom of hypertension, must be considered incomplete congenital glaucomas, according to Kluyskens.

Let us add, by way of conclusion:

That the anomalies of the iridocorneal angle constitute the common denominator of different diseases which are apparently independent of each other but which are undoubtedly related and may be interpreted as various states of ocular malformation.

That, the different types of gonioscopic anomalies appear to imply, when they are very evident, a certain index of seriousness in the disease.

That the alteration of the ocular tension, which has been considered the outstanding sign for diagnosis in congenital glaucoma, today must be taken as a typical modality in the evolution of all these conditions, the appearance of which may or may not occur but which obviously, when present, is one of the salient symptoms, and possibly the one to play the most important role in the evolution of the disease.

That although we have not had the opportunity to observe pure megalocornea without abnormalities at the angle, we accept its probable existence; however, the few examples to be found in the literature are not, in our opinion, too convincing.

That we accept the term, incomplete congenital glaucoma, or pure hydrophthalmos, for all the megalocorneas we examined, since they offered the three essential signs proposed by Kluyskens and were not complicated by ocular hypertension.

That ocular hypertension, in association with abnormalities at the angle, is sufficient to warrant a diagnosis of complete congenital glaucoma, the corneal diameter not being an essential attribute to this classification, since the disease can occur with a normal corneal diameter (Case 9).

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ISHIHARA TEST IN COLOR-VISION DEFECTS*

Studies on a statistical method for evaluation of the screening efficiency of several plates

Akira Nakajima, M.D., Hiroshi Ichikawa, M.D., and Osamu Nakagawa, M.D.
Tokyo, Japan
Akio Majima, M.D.
Nagoya, Japan
and
Masanobu Watanabe, M.D.
Shizuoka, Japan

1. Introduction

The Ishihara test has been used all over the world as a standard test for screening red-green color vision defects since 1933. However, recently a trade union criticized this test for screening "too many color blinds" among its members.

Although the ability of this test for the screening of color vision defects has been confirmed from time to time by many authors, this episode pointed to a fairly widespread misconception that any misreading of any plates in the Ishihara or other tests is due to some defect in color vision. As frequently shown by many studies (Hardy, et al., 1946, Kettesy, 1955, Ichikawa, 1957, Belcher, et al., 1958), not one of the plates in any existing test is perfect in the sense that all normals read normally and all those with color vision defects read like color defectives under all circumstances.

In other words, screening with any one plate is accompanied by a certain amount of error, and statistical treatment of the result obtained by several tests is essential to reliable screening. Although this fact has been shown by many authors, so far no one has attempted to investigate the theoretical background which would enable an examiner to plan and predict the efficiency of the screening by any set of pseudo-isochromatic plates.

Prof. S. Ishihara had intended to publish a version of his test which had been abridged without decreasing its screening efficiency, and, when we had an opportunity to make detailed ophthalmic examinations on 3,000 school children being subjected to a consanguinity study, this abridged version (13th edition) was used for screening color-vision defects, along with detailed anomaloscopic examination of those who were picked up by the screening. A part of the result has already been published elsewhere (Majima, et al., 1959). The basic principle of the screening of color vision defects by a set of plates will be described in this study, taking the result of the survey as an example. This should provide a basis for evaluation of any existing test on a practical basis, and would permit detailed analyses of various factors involved in the problem.

* From the Department of Ophthalmology, Juntendo University, Tokyo, the Department of Ophthalmology, Nagoya University, Nagoya, the Eye Clinic, Central National Railroad Hospital, Tokyo, and the Eye Clinic, Saiseikai Hospital, Shizuoka.

TABLE 1

NUMBER OF CHILDREN EXAMINED DURING THE 1958 SURVEY AT SHIZUOKA

Grade	1	2	3	4	5	TOTAL
M	124	149	410	403	438	1,524
F	120	135	400	394	460	1,509
TOTAL	244	284	810	797	898	3,033

2. MATERIAL AND METHOD

Detailed ophthalmic examinations (table 2) were carried out on 3,033 school children aged from six to 10 (table 1) years. These children were from two primary schools in the central part of Shizuoka which has nearly 300,000 inhabitants. This survey was performed as a part of research on the effect of consanguinity, and various other tests were carried out at the same time. The survey took place during the summer vacation in 1958. About 50 children were brought by bus every afternoon to Saiseikai Hospital where all medical examinations were carried out and returned by bus after all examinations were finished. Some of the children were brought to the hospital at a later date for re-examination. The whole survey took about two months. The result of the survey, other than described herein, especially the prevalence of various anomalies of the eye among Japanese children, will be published as a later study.

The system of the examination for color vision was: 25 plates were selected for this study from the newest (13th) edition of the Ishihara test by the Committee on Color Blindness.* The eight plates for illiterates were not used at all, as none of the children examined was illiterate. One additional plate (No. 1) can be read by color-vision defectives. In all, 16 plates were used for the screening. In addition to the Ishihara test, which is designed for the screening of red-green defects, two plates for the screening of tritanopes in Hardy-Rand-Rittler test were used together with a plate specially drawn for this purpose by Dr. Okayasu. Not one of the 3,033 children misread these plates for tritanopes.

All tests were done under artificial illuminant-C. Every reading was recorded and subjected to detailed analysis. Anomaloscopic examination was performed on 80 children who misread more than nine out of 16 plates and 18 out of 27 children who misread between four and eight plates out of 16. Among the latter children, eight who had misread four plates were re-examined by all plates of the Ishihara and Hardy-Rand-Rittler tests, which showed them to be normal (no misreading on re-examination). Only one child who had misread seven plates could not be traced because of moving out of the city. Two anomaloscopes, Nagel type and Hioki type (Hioki, 1955), were used. Nine normal and 24 color-vision defectives were first examined twice by the different types of anomaloscope at the same time; after seeing no dis-

* Committee for the Improvement of the Ishihara Test. Office at the Department of Ophthalmology, Juntendo University, Tokyo.

TABLE 2

THE SYSTEM OF OPHTHALMIC EXAMINATIONS OF THE SURVEY

1. Visual acuity and refractive error
   3 test types (one for illiterates): natural illumination (500–3,000 lux)
   2 assistants, a set of lens plates
2. Color vision
   25 selected plates from the newest (13th) edition of Ishihara test (7 plates are for illiterates): artificial illuminant-C: Plate No. 5 and 6 of HRR test, a plate made by Dr. Okayasu: one assistant: anomaloscopic test for suspective color vision defectives (two instruments) anomaloscopic examination performed by Dr. Ichikawa, Dr. Majima, and Dr. Nakajima.
3. Routine ophthalmic examinations (objective) done by Dr. Majima.
   Cover test for phoria and tropia: oblique illumination with magnifier: ophthalmoscopic examination: photographic recording of the selected findings by fundus (done by Dr. Baba).

TABLE 3

THE DISTRIBUTION OF MISREADINGS OF ISHIHARA TEST

a. NORMALS

Number of Plates Misread	Grade						Total No. of Plates Misread
	1	2	3	4	5	Total	
0	120	131	458	504	697	1,910	0
1	46	80	211	187	132	656	656
2	35	41	88	63	36	263	526
3	20	23	28	19	7	97	291
4	7	6	6	1	0	20	80
5	1	1	2	1	0	5	25
6	0	0	0	0	0	0	0
7	0	0	0	1*	0	1	7
8	0	0	0†	0	0	0	0
Total	229	282	793	776	872	2,952	1,585
Total No. of plates (aver./person)	209	260	503	386	225	1,585	—
	0.857	0.915	0.624	0.484	0.250	0.553	(unexpected R. 0.484: expected R. 0.069)

* Could not be re-examined, but classified as normal.
† One who misread eight did not misread on immediate re-examination, and classified as 0.

b. COLOR VISION DEFECTIVES

Number of Plates Misread	Type of Color Vision Defects					No. of Plates Misread
	Da	D	Pa	P	Total	
6	0	0	1	0	1	6
7	0	0	0	0	0	0
8	0	0	0	0	0	0
9	2	0	0	0	2	18
10	0	0	1	0	1	10
11	1	1	1	0	3	33
12	2	0	0	0	2	24
13	4	1	2	0	7	91
14	4	6	1	0	11	154
15	11	7	0	0	18	270
16	10	21	1	4	36	576
Total	34 (42.0%)	36 (44.4%)	7 (8.6%)	4 (5.0%)	8	1,182
Male	31	35	7	4	77	
(%)	2.1%	2.23%	0.46%	0.26%	5.05% of total males	
Female	3	1	0	0	4	
(%)	0.19%	0.07%	0%	0%	0.26% of total females	
Aver. misread exp.	10.9	13.8	8.8	10.8	11.9	
unexp.	3.4	1.4	3.0	5.3	2.5	
Total	14.3	15.2	11.8	16.0	14.4	

crepancy in the result by two instruments, each instrument was used separately.

3. RESULTS

The results are summarized in Tables 3 to 7. Table 3-a and b show the number of misreadings for normal and color-vision defective subjects. As can be seen from Table 3, normal children misread a certain number of plates, the average being 0.5 plate out of 16, but the manner of misreading usually was neither that expected for color vision defectives (expected response) nor normals (normal response); this is called herein the "unexpected response." Nearly 90 percent of the misreadings by normals are "unexpected responses."

It is interesting to note that this ratio is about the same for all age groups, although the average number of misreadings decrease as the age increases. The distribution of the number of misreadings has very distinct

maxima at both ends, zero and 16, and there are only a few children who misread between four and 10 plates, the number of children in this group being only about one percent of the whole population. All children who misread more than nine plates proved by the anomaloscope to have color-vision defects of various kinds, though no clear-cut correlation could be observed between the number of misreadings and equation range. Only one among those who misread between four and eight plates proved to be a color vision defective (protanomalous).

Although anomaloscopic examination was not performed on the group misreading zero to three, the probability that this group contains any color vision defective is practically negligible for reasons which will be given later.

Thus, our results show that color-vision defectives can be clearly separated by the test described here, if the number of misreadings is used as the criterion. It shows further that those with more than nine misreadings in this set of plates are color-vision defectives, those misreading less than three definitely normal, and those with an in-between number of misreadings doubtful.

Table 4 presents the manner of misreading for each plate found in the survey. Some mistakes are found solely in normals or color vision defectives, and others are found in both (overlapped responses). Although this table by no means covers every possible way of reading for each plate, it may be regarded as a fairly thorough table in view of the fact that the subjects were school children among whom the number of misreadings is considered to be much higher than among adults.

Table 5 gives the actual number of misreadings for the individual plates, classifies them into normal, expected, unexpected not overlapped, and unexpected overlapped. It will be seen from this table that some plates, for example, No. 4, have a large number of misreadings in "unexpected overlapped" response for both normals and color-vision defectives, whereas one plate (No. 9) has a high number of misreadings in "unexpected not overlapped" response in normals. Plates No. 2 and No. 3 have a high proportion of normal responses in color-vision defectives. Thus, this table indicates fairly clearly the features of the misreadings for each plate.

Table 6 was made from Table 5 to show the features of the individual plates. The error coefficients, the definition of which is

TABLE 4

MANNER OF RESPONSES FOR EACH PLATE

Plate No.	Responses				
	Normal	Unexpected for normal	Overlapped Response	Unexpected for Color Defect	Expected
2	8	x, 2	—	—	3
3	6	9	—	—	5
4	29	19, 30, 71, 26, 3, 6, 0, 7, 9	20, 7	10, 80, 90	70
6	5	3, 6, 0, 7, 9	8, x	1	2
8	15	16, 75, 5	x	11, 27, 25, 19, 7, 4, 29, 12, 1	17
9	74	14, 24, 54, 71, 76, 17, 94, 91, x4, 20, 70	x	87, 1, 25, 2	21
10	2	8, 9	—	6	x
11	6	5, 18, 8, 15, 9	0	3	x
13	45	75, 10, 25, 6, 76, 46, 16, 48, 95	15, 16, x5	17, 27	x
14	5	6, 10, 9	—	0, 38	x
15	7	—	9, 2	3, 10, 1	x
16	16	10, 18, 56, 76, 26	6	35	x
18	x	11	7	6, 15	5
20	x	41, 46, 16, 47, 43	—	5, 4, 10, 15, 14, 42, 65	45
22	26	21, 25, 86	28, 20, 36	2, 22, 27, 8, 88, x	2, 6
24	35	85, 56, 28	8, 36, 65	32, 95, 6, 30, 33, 38, x	3, 5

x = cannot recognize digit.

TABLE 5

MISREADINGS OF INDIVIDUAL PLATES

Plate No.	Normal				Color-Vision Defects							
					a					b_1	b_2	c
	A	B_1	B_2	C	Da	D	Pa	P	Total			
2	2,950	2	0	0	9	6	3	0	18	0	0	63
3	2,950	2	0	0	16	12	4	0	32	0	0	49
4	2,382	6	564	0	2	0	0	0	2	19	14	46
6	2,835	72	43	2	1	0	0	0	1	14	1	65
8	2,945	4	2	1	3	2	1	0	6	5	28	42
9	2,508	416	6	22	0	0	0	0	0	2	6	73
10	2,868	19	0	65	1	1	1	0	3	0	1	77
11	2,910	19	4	19	3	1	1	0	5	1	1	74
13	2,845	58	25	24	1	0	1	0	2	3	2	74
14	2,931	4	0	17	1	0	2	0	3	0	2	76
15	2,945	0	5	2	1	0	2	0	3	2	5	71
16	2,863	61	1	27	1	0	4	0	5	1	1	74
18	1,937	1	3	11	5	0	2	0	7	1	3	70
20	2,941	6	0	5	4	3	2	0	9	0	12	60
22	2,917	4	30	1	2	1	2	0	5	14	7	55
24	2,921	13	17	1	8	1	4	0	13	5	8	55
TOTAL		687	700	198 (1,585)	58	27	29	0	114	67	91	1,024 (1,296)
MEAN	2,852.9	42.8	43.9	12.4	3.6	1.7	1.8	0	8.4	3.3	5.3	64.0

A: normal responses of normal; B_1: unexpected not overlapped responses of normal; B_2: unexpected overlapped responses of normal; C: expected responses of normal; a: normal responses of color-vision defects; b_1: unexpected overlapped responses of color-vision defects; b_2: unexpected not overlapped responses of color-vision defects; c: expected responses of color-vision defects.

given below the table, are the ratio of the proportion of erroneous responses to correct ones. The difference between E_1, E_2, and E_3 is due to the difference in the definition of correct and erroneous responses. In E_1, all responses other than normal response in normal children and all responses other than expected responses in color-vision defective children are regarded as erroneous responses; whereas, in E_3, only expected responses in normals and normal responses in color-vision defectives are regarded as erroneous responses. According to the definition of error coefficients, plates with smaller error coefficients are of better quality. It will be seen from Table 6 that plates from 10 to 18 are good, whereas plates from 2 to 8 and 22, 24 are not so good.

Although these coefficients indicate the quality of each plate, they themselves have no immediate practical application. On the other hand, the probability of misreadings, which are given in the same table (table 6), is useful for evaluation and planning of screening for the reason to be described. For screening, it is practical to classify the manner of reading into two—normal and erroneous—responses. Every pseudo-isochromatic plate is not intended to be read by color-vision defectives as normal subjects would read it; the normal response by any color vision defective should be regarded as an error. Consequently, the probability of misreadings given in Table 6 is the probability of reading other than normal for normal, and that of normal reading for color vision defects. As shown in the table, there seems to be a tendency for p_{cd} to be large when p_n is small or vice versa, but this tendency is by no means constant, and in some plates both are small, showing the superior quality of the plates.

Plates No. 22 and 24 were originally designed to separate protanopes from deutanopes. The results in this respect were rather disappointing and the details will not be given here. The analysis in relation to sex showed no interesting result.

TABLE 6

ERROR COEFFICIENTS AND PROBABILITY OF MISREADINGS

Plate No.	Error Coefficients			Probability of Misreadings					Color-Vision Defectives
	E_1	E_2	E_3	Normal	Da	D	Pa	P	
2	12.5	12.5	12.5	.1	26.4	16.6	42.8	0	22.2
3	24.7	24.6	24.6	.1	47.0	33.3	57.2	0	39.5
4	45.5	29.2	1.3	19.3	5.7	0	0	0	2.5
6	13.6	11.1	.7	4.0	2.9	0	0	0	1.3
8	31.9	8.8	3.8	.2	8.8	5.5	14.3	0	7.4
9	14.3	1.7	.4	15.0	0	0	0	0	0
10	4.0	3.0	3.0	2.8	2.9	2.7	14.3	0	3.7
11	5.2	4.3	3.5	1.4	8.8	2.7	14.3	0	6.2
13	6.6	4.0	1.7	3.6	2.9	0	14.3	0	2.5
14	3.6	2.2	2.2	.7	2.9	0	28.6	0	3.7
15	6.7	3.3	1.9	.2	2.9	0	28.6	0	3.7
16	6.1	4.4	3.7	3.0	2.9	0	57.2	0	6.2
18	7.6	5.5	4.7	.5	14.7	0	28.6	0	8.6
20	16.0	4.6	4.6	.4	11.8	8.3	28.6	0	11.1
22	36.6	10.0	.6	1.2	5.7	2.7	28.6	0	6.2
24	33.7	3.5	1.3	1.1	23.5	2.7	57.2	0	16.0
				3.4	10.6	4.7	25.9	0	7.1

$$E_1=[(B_1+B_2+C)/Tn+(b_1+b_2+a)/Tcvd.]/\frac{A}{Tn}+\frac{c}{Tcvd},\quad E_2=\frac{\frac{B_2+C}{Tn}+\frac{b_1+a}{Tcvd}}{\frac{A+B_1}{Tn}+\frac{b_2+c}{Tcvd}}$$

$$E_3=\frac{\frac{C}{Tn}+\frac{a}{Tcvd}}{\frac{A+B_1+B_2}{Tn}+\frac{c}{Tcvd}}$$

$$Tn=A+B_1+B_2+C$$

$$Tcvd=a+b_1+b_2+c$$

4. STATISTICAL ANALYSIS OF MISREADINGS OF PLATES

The results presented indicate that the test using 16 plates from the 13th edition of the Ishihara test can separate color-vision defectives from normal subjects almost perfectly, provided that the plates are used as a set, and the number of misreadings is taken as the criterion. As shown in Table 6, not one plate is perfect in itself; and errors will result if they are used individually. Our results show further that, if a set of 16 plates is used for screening, those who misread more than nine are color-vision defectives, whereas those with less than three misreadings are normal. Those whose misreadings fall between three and nine, although they are small in number, should be examined by other methods, such as by the anomaloscope.

It would be convenient if the result of screening by any set of plates arbitrarily chosen from any test could be predicted, the efficiency and error being capable of estimation beforehand. Statistical treatment is indispensable to such a purpose. The distribution of the number of misreadings of a set is related to the probability of misreadings for the individual plates making up the set. The statistical relationship which correlates these two is as follows:

If p_i ($i = 1, 2, —, m$) represents the probability of misreading for plate i in a set of m plates, the probability for a person to misread r plates in a set of m plates is, according to the theory of probability, the sum of the multiple of p_i for r different plates and $1 - p_i$ ($=q_i$) for the remaining $m - r$ plates, the sum being taken for all possible combinations. In special cases where p_i is equal for all plates, the above probability will be $\binom{n}{r} p^r q^{m-r}$.

In more specific cases where p_i can be re-

garded as small and m as large, the distribution will follow Poisson's distribution.

Here, it should be borne in mind that these relationships are based on the assumption that p_i can be defined as a uniform characteristic of the population concerned (Snedecor, 1940). If a population concerned is made up of several subgroups which have uniform p_i within each subgroup but have different values of p_i between subgroups, this formula will hold only within each subgroup, and the distribution of misreadings for the whole population will be the sum of the distribution for each subgroup constituting the population.

This feature can be used for the test of uniformity of a population as to the probability of misreadings. For example, the distribution of misreadings presented in Table 3 does not follow the distribution just cited because this population is composed of at least two subgroups, normals and color-vision defectives.

Table 7 gives the observed distribution of misreadings for normal and three kinds of color-vision defects, compared with the Poisson distribution which is calculated using the observed values. It will be seen that both fit fairly well, indicating that the Poisson distribution can be used for the approximation of the observed distribution. However, closer observation of the table reveals that the figures of the theoretical distribution are smaller in misreading 0, whereas they are larger in misreading 1 in every group; this would indicate the existence of subgroups which could not be separated even by the anomaloscope. The discrepancy is less marked in the distribution for each age group than in that for the total normals. For the groups of color-vision defectives, both distributions show fairly good accord in spite of the fact that the size of the population is much less than that of the normal.

On the whole, it can be stated that the Poisson distribution can serve as a fairly good approximation for the distribution of misreadings for each subgroup of the population studied. This situation may be understandable if we think of the complicated fac-

TABLE 7

DISTRIBUTION OF MISREADINGS AND POISSON DISTRIBUTION

Grade		Number of Misreadings						Average
		0	1	2	3	4	5	
				1. Normal				
1–2	obs.	251	126	76	43	13	2	0.9
	calc.	219	187	84	25	6	1	0.9
3	obs.	458	211	88	28	6	2	0.6
	calc.	434	261	78	16	2	0	0.6
4	obs.	504	187	63	19	1	1	0.5
	calc.	470	235	59	10	1	0	0.5
5	obs.	697	132	36	7	0	0	0 3
	calc.	645	194	29	3	0	0	0.3
				2. Color-vision Defectives				
Da	obs.	0.29	0.33	0.13	0.13	0.06	0.03	1.7
	calc.	0.18	0.31	0.26	0.15	0.06	0.02	1.7
D	obs.	0.55	0.19	0.16	0.03	0	0.03	0.8
	calc.	0.45	0.36	0.14	0.04	0.01	0.001	0.8
Pa	obs.	0.14	0	0.14	0.28	0	0.14	4.2
	calc.	0.01	0.06	0.13	0.18	0.19	0.16	4.2

(Poisson distribution calculated from Marcel Boll: Tables Numérique Universélles, 1957, p. 672.

tors involved in misreadings in addition to the pattern of the plate and color sense of subject; and the same situation exists for traffic or industrial accidents which usually follow Poisson distribution.

On the assumption that the distribution of misreadings follows Poisson distribution, the probability for the normal to misread more than seven out of 16 plates is calculated to be about one millionth, which is negligible for practical purpose. In an adult population, which is supposed to have much smaller probability of misreadings than school children, this will be still smaller. On the other hand, if the misreadings in color-vision defectives are assumed to follow Poisson distribution, the probability of protanomalous having more than seven misreadings (normal reading is referred to as misreading in color-defective groups) is about seven percent, and deuteranomalous about 0.2 percent. The probability of anomalies in a normal group, misreadings of more than 13, is about 1:10,000 for protanopes and nil for deuteranopes. An error of this order should be negligible for any practical purpose.

If a set of different plates is used for screening, the screening efficiency and error of the set can be calculated beforehand from the probability of misreading of each plates constituting the set. For example, for a set of three plates, consisting of No. 8, No. 14 and No. 15 of the 13th edition of the Ishihara test, the probability for normals to misread 0, 1, 2, or 3 plates is calculated respectively as 98.9, 1.1, 3×10^{-3} and 6×10^{-6} percent on the basis of the figures given in Table 6. The probability for color-vision defectives to make normal readings, obtained in the same way, is 84, 15, 0.7 and 1×10^{-2} percent, respectively. If the fiducial limit of the probability at the one-percent level (Snedecor, 1940) in Table 6 is taken into consideration, this becomes in most favorable cases, 99.7, 0.3, 6×10^{-5} and 10^{-9} percent, in most unfavorable cases, 97.9, 2.1, 1.5×10^{-3}, and 2×10^{-5} percent, respectively, for normals. For color vision defectives, in most favorable cases, 97.7, 2.1, 1.5×10^{-3}, and 2×10^{-6} percent and in most unfavorable cases, 66.0, 26.6, 4.8 and 2.6 percent, respectively. Namely, if one misreading is allowed for normals, the probability for normals to be in a color-vision defective group is negligible; at the same time up to 7.0 percent of color-vision defectives may be regarded as normal by this set of screening plates. This kind of estimation will become more accurate if p_i for each plate is determined from the result of more than one thousand trials for each type of color-vision defect, as well as normal. The estimation of p_i in a large population may not be so difficult if the results obtained on many occasions are pooled for this purpose. If any discrepancy is found among the results thus gathered, it will indicate the necessity of detailed analysis of the cause of the discrepancy, and the information obtained from the study will be important for the improvement of the method of screening color-vision defects, as well as of the method of classification of color-vision defects.

5. Summary

A set of Ishihara test plates (25 selected plates out of the 13th edition of the test) were used for the screening of color-vision defects in 3,033 school children aged from six to 10 years, along with three other plates for tritanopes and anomaloscopic examination for defectives picked up by the screening. Using the number of misreadings of the plates as criterion, this set of Ishihara test plates could separate red-green defectives very clearly from normals. Eighty children who misread more than nine plates were all color-vision defective, and among those who misread between four and eight plates only one (who misread six) proved to be protanomalous by anomaloscopic examination. The analysis of the distribution of misreadings by statistical methods was presented. The Poisson law can be used for the approximation of the observed distribution, and the efficiency and error of screening can be estimated on this basis. It was shown further

that the probability of misreading for an individual plate is useful for planning and estimating the efficiency and error of screening by a number of plates arbitrarily chosen from the original testing set.

Department of Ophthalmology,
Juntendo University.

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THE EFFECT OF CARBONIC ANHYDRASE INHIBITORS ON URINARY EXCRETION OF CITRATE BY HUMANS*

MARGUERITE A. CONSTANT, PH.D., AND BERNARD BECKER, M.D.
Saint Louis, Missouri

The occurrence of ureteral colic in glaucoma patients on long-term acetazolamide therapy has stimulated interest in their urinary citrate excretion. The oral administration of the carbonic anhydrase inhibitor, acetazolamide, has been found by several investigators[1-3] to decrease markedly the urinary citrate excretion of humans. Recently other potent carbonic anhydrase inhibitors, such as methazolamide and dichlorphenamide, have been added to the armamentarium of ophthalmologists. It was of interest to determine whether these newer drugs had a similar effect on urinary excretion of citrate.

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MATERIALS AND METHODS

The subjects were ambulatory and no special dietary restrictions were made. Twenty-four hour urine collections were made under toluene for a single collection period before and two consecutive periods after the oral administration of acetazolamide,* methazolamide* or dichlorphenamide.† Aliquots were stored at −20°C. until analyzed. Citrate was determined by the method of Ettinger, et al.[4]; creatinine by the alkaline picrate method, uric acid by arsenomolybdate method[5]; pH, ketones, proteins and glucose with pH Hydrion paper, Ketostix and Uristix (Ames Co.), respectively.

RESULTS AND DISCUSSION

Acetazolamide (table 1), 250 mg. q6h for for 24 hours, decreased urinary citrate ex-

* Acetazolamide (Diamox®) and methazolamide (Neptazane®) were kindly supplied by American Cyanamid Company.

† Dichlorphenamide (Daranide®) was kindly supplied by Merck, Sharp & Dohme Company.

TABLE 1

THE EFFECT OF ACETAZOLAMIDE ON THE URINARY EXCRETION OF CITRATE BY HUMANS

Subject	Drug Administration (hr.)	Volume (ml.)	Creatinine mg./24 hr.	Citrate mg./24 hr. (C)	ΔC %	Citrate: Creatinine Ratio (R)	ΔR %	pH
			Acetazolamide—250 mg.—Single dose					
*	0	1,275		504				
	24	1,610		190	−62			
			Acetazolamide—250 mg. q6h—long-term administration					
*		1,224		34	(−94)			
			Acetazolamide—250 mg. q6h					
#1	0	700	810	275		0.34		6.2
	24	470	350	76	−72	0.22	−35	8.0
	48	525	244	44	−84	0.18	−47	7.2
#2	0	1,330	2,182	825		0.38		6.2
	24	2,030	2,770	233	−72	0.08	−79	9.0
	48	640	1,010	106	−87	0.10	−74	7.0

* Shah, *et al.*, 1958—average value for 10 patients.

cretion by an amount (72 percent) similar to that found previously (62 percent)[3] after a single 250-mg. dose. Continued administration for another 24 hours reduced citrate excretion further (by 86 percent) or almost as low (approximately 94 percent) as seen after long-term therapy.[3] Methazolamide (table 2), 100 mg. q8h, had less effect during the first 24 hours, reducing citrate excretion by an average of 40 percent. After 48 hours the urinary citrate level was reduced by approximately 69 percent compared to pretreatment levels. Dichlorphenamide (table 3), 50 mg, q6h or 100 mg. q8h,

TABLE 2

THE EFFECT OF METHAZOLAMIDE (100 MG. Q8H) ON THE URINARY EXCRETION OF CITRATE BY HUMANS

Subject	Drug Administration hr.	Volume ml.	Creatinine mg./24 hr.	Citrate mg./24 hr. (C)	ΔC %	Citrate: Creatinine Ratio (R)	ΔR %	pH
#3	0	520	790	500		0.63		6.0*
	24	460	388	159	−68	0.41	−35	7.2
	48	1,040	1,390	298	−40	0.21	−87	6.4
#4	0	1,050	780	417		0.53		6.0*
	24	870	795	181	−57	0.23	−57	6.5
	48	950	754	17	−96	0.02	−96	6.2
#5	0	870	1,045	275		0.26		6.0*
	24	1,250	800	192	−30	0.24	− 8	7.3
	48	630	435	74	−73	0.17	−35	7.2
#6	0	330	480	125		0.26		8.0
	24	830	795	104	−17	0.13	−50	9.0
	48	430	480	54	−57	0.11	−58	9.0
#7	0	570	455	148		0.33		6.8
	24	430	540	105	−29	0.19	−42	6.0*
	48	500	510	33	−78	0.06	−82	6.0*
Ave. (5)	0			293		0.40		6.6
	24			148	−40	0.24	−38	7.2
	48			95	−69	0.11	−72	7.0

* Urine pH of 6.0 was between 5.5 and 6.0.

TABLE 3

THE EFFECT OF DICHLORPHENAMIDE (50 MG. Q6H* OR 100 MG. Q8H†) ON THE URINARY EXCRETION OF CITRATE BY HUMANS

Subject	Drug Administration hr.	Volume ml.	Creatinine mg./24 hr.	Citrate mg./24 hr. (C)	ΔC %	Citrate: Creatinine Ratio (R)	ΔR %	pH
#8*	0	760	990	293		0.30		6.0
	24	1,040	332	66	−78	0.20	−33	7.2
	48	1,180	893	72	−76	0.08	−73	6.8
#9*	0	400	417	150		0.36		6.2
	24	2,200	856	200	+33	0.23	−36	7.8
	48	1,650	903	36	−76	0.04	−89	7.8
#10*	0	1,870	1,392	310		0.22		6.0
	24	580	187	37	−88	0.20	− 9	7.4
	48	800	560	44	−86	0.08	−64	7.6
#11*	0	620	930	1,062		1.14		6.0
	24	1,400	734	207	−80	0.28	−76	9.0
	48	870	620	113	−82	0.18	−84	8.0
#12†	0	1,875	1,230	779		0.63		7.0
	24	1,925	1,080	224	−69	0.23	−64	9.0
	48	595	506	109	−86	0.22	−65	7.5
#13†	0	1,830	1,340	160		0.12		6.0
	24	1,650	910	28	−83	0.03	−75	7.6
	48	1,310	880	59	−63	0.07	−42	7.2
Ave.(3)*	0			251		0.29		6.0
	24			101	−60	0.21	−26	7.5
	48			51	−80	0.07	−75	7.4
Ave. (3)†	0			667		0.63		6.3
	24			160	−76	0.18	−72	8.5
	48			94	−86	0.11	−83	7.5

* Urine pH of 6.0 was between 5.5 and 6.0.

reduced citrate excretion by an average of 60 or 76 percent, respectively, during the first 24 hours, and the excretion was slightly lower during the second 24-hour period, being decreased by approximately 80 to 86 percent.

Because of the decrease in urine volume during the experimental periods compared to that of the control period in several instances, and the marked diuresis in others, it was felt that the citrate: creatinine ratios might more nearly reflect the alteration in the citrate excretion. The data so calculated (tables 1, 2, and 3) gave results in most instances similar to those obtained from the citrate excretion data alone. After 100-mg. doses of methazolamide or 50-mg. doses of dichlorphenamide, the citrate to creatinine ratio was decreased by an average of only 38 or 26 percent, respectively, during the first 24 hours, but was decreased during the second 24-hour interval by approximately 72 to 75 percent. The larger dose of dichlorphenamide (100 mg. q8h) decreased citrate excretion by 72 percent on the basis of citrate:creatinine ratio during the first 24 hours and 83 percent during the second 24-hour period.

Random samples of urine from two clinic patients on dichlorphenamide therapy (100 mg. q8h) for several months presented citrate concentrations of 7.0 and 11 mg. percent and citrate:creatinine ratios of 0.07 and 0.06. These values are similar to mean values of 10± (S.D.) 4.0 mg. percent found previously in long-term acetazolamide therapy, and very different from the average values of glaucoma patients treated with miotics

alone (60± 25 mg. percent).[3]

The present studies confirmed the previous findings[3] and the results of other investigators[1,2] that oral acetazolamide administration caused a marked decrease in urinary citrate excretion by humans. In view of the complex action of citrate with calcuim, the continued minimal excretion of citrate by patients on acetazolamide therapy may increase their susceptibility to calculi formation.[6] In some glaucoma patients on long-term therapy with acetazolamide, temporary relief of ureteral colic occurred when methazolamide was substituted for acetazolamide.[7] This observation suggested the possibility that other carbonic anhydrase inhibitors might not cause such a marked decrease in citrate excretion. Unfortunately, the results of the present studies indicated that the three potent carbonic anhydrase inhibitors, acetazolamide (250 mg. q6h), methazolamide (100 mg. q8h) and dichlorphenamide (50 mg. q6h or 100 mg. q8h) were equally effective in decreasing citrate excretion by humans.

In these studies no correlation between the degree of alkalinization of the urine and citrate excretion was apparent. Citrate excretion was further decreased during the second day of carbonic anhydrase administration although the urine pH was returning to or had returned to normal values. The independence of citrate excretion and urine pH has been reviewed by Milne, et. al.[8] No abnormalities were noted in the excretion levels of ketones, glucose or protein. One patient presented slightly more than 30 mg. percent of protein in the urine but the change in citrate excretion level after administration of a carbonic anhydrase inhibitor was similar to that of other patients who had negative tests for protein.

Concurrent studies evaluating various therapy in the glaucoma clinic provided an opportunity to study the recovery of citrate excretion after discontinuing acetazolamide administration. These data (table 4) indicated that the citrate excretion level of patients who had not received acetazolamide for one week had not returned to normal values. The excretion level of citrate averaged 52 mg./24 hr. which was not significantly different from the average of 34 mg./24 hr. for patients on long-term therapy. Compared to an average normal excretion level of 457 mg./24 hr. in our series of 23 subjects, the citrate excretion of these patients continued to be decreased by some 89 percent for at least one week.

Although approximately 90 percent of an orally administered dose of acetazolamide to man was found to be excreted in the urine in 24 hours[9] the decreased citrate excretion of patients on long-term therapy lasted at least one week after discontinuing therapy. On the other hand, the citrate excretion of rats

TABLE 4

RECOVERY OF CITRATE EXCRETION AFTER DISCONTINUING ACETAZOLAMIDE THERAPY*

Subjects	Duration of Therapy Days	Urine Volume ml.	Citrate mg./24 hr.	Creatinine mg./24 hr.	Citrate: Creatinine Ratio	pH
#14	0	780	35	694	0.05	6.0
#15	0	1,194	56	912	0.06	5.7
#16	0	770	79	770	0.10	6.4
#17	0	1,990	39	868	0.04	6.2
Ave. (4)	0	1,184	52	811	0.06	—
†	0	1,275	504	—	—	—
†	Long-term	1,224	34	—	—	—
‡	0	979	409	911	0.45	—
‡	2	855	99	704	0.14	—

* Acetazolamide, 250 mg. every 6 hr., which had been administered for several months, was stopped for one week prior to obtaining the urine sample.

† Mean value for 10 patients—Shah, *et al.*, 1958.

‡ Present study—mean value for 13 patients.

TABLE 5

THE EFFECT OF CARBONIC ANHYDRASE INHIBITORS ON URIC-ACID EXCRETION BY HUMANS

Subject and Drug	Duration of Therapy hr.	Urine Volume ml.	Uric Acid mg./24 hr.	Experimental/Control	
				Uric Acid	Uric Acid: Creatinine
#1 Acet.	0	700	396	—	—
	24	470	157	0.40	0.92
	48	525	119	0.30	1.00
#2 Acet.	0	1,330	674	—	—
	24	2,030	455	0.68	0.52
	48	640	255	0.38	0.82
#3 Meth.	0	520	408	—	—
	24	460	233	0.55	1.10
	48	1,040	817	2.00	1.13
#4 Meth.	0	1,050	346	—	—
	24	870	394	1.14	1.14
	48	950	447	1.29	1.34
#5 Meth.	0	870	561	—	—
	24	1,250	328	0.59	0.76
	48	630	212	0.38	0.91
#6 Meth.	0	330	216	—	—
	24	880	348	1.61	0.98
	48	430	174	0.81	0.80
#7 Meth.	0	570	285	—	—
	24	430	267	0.94	0.78
	48	500	187	0.66	0.59
#8 Dcp.	0	760	512	—	—
	24	1,040	146	0.29	0.85
	48	1,180	565	1.10	1.21
#9 Dcp.	0	400	156	—	—
	24	2,200	276	1.77	0.84
	48	1,650	415	2.56	1.21
#10 Dcp.	0	1,870	586	—	—
	48	880	206	0.35	0.88
#11 Dcp.	0	620	755	—	—
	24	1,400	234	0.31	0.40
	48	870	298	0.40	0.59
#12 Dcp.	0	1,830	570	—	—
	24	1,650	348	0.61	0.88
	48	1,310	393	0.69	1.04
#13 Dcp.	0	1,875	194	—	—
	24	1,925	175	0.90	1.00
	48	595	126	0.65	1.56
Average (13)	0		435	—	—
	24		280	0.64	0.83
	48		324	0.74	0.96

Acet. = Acetazolamide; Meth. = methazolamide; Dcp. = dichlorphenamide.
These are the same patients as listed in Tables 1, 2, 3.

fed a natural diet containing acetazolamide (daily intake of approximately 50 mg./kg.) for a period of three to four weeks was markedly decreased but recovered to normal levels immediately after withdrawal of the drug.[10] Harrison and Harrison[11] found renal lesions in rats fed an acetazolamide containing semisynthetic diet with Ca and P im-

balance but determined the recovery phase (which was immediate) only after short-term (four days) acetazolamide administration. This lasting effect of carbonic anhydrase inhibitors on depressing urinary citrate excretion after discontinuing the drug is under further study.

During analyses of urines, differences in quantities of a white sediment were observed, suggesting a possible effect of the drug. Because solubility characteristics were suggestive of uric acid, the concentration of this compound was determined in all urines (table 5). In eight of 13 urines of the first 24 hours during drug administration the total uric acid was decreased by 32 to 71 percent with an average decrease for the group of 36 percent. During the second 24-hour period the total uric acid excretion was decreased by some 31 to 70 percent in eight of 13 subjects with an average of 40 percent. On the basis of the uric-acid to creatinine ratio, however, an effect was less evident with an average decrease of 17 percent during the first 24 hours and four percent during the second 24 hours of drug administration. Analyses of plasma of glaucoma patients who had been off therapy for one week were made four hours after the oral administration of carbonic anhydrase inhibitors. These data failed to reveal any consistent change in their plasma uric-acid level.

Summary

The effect of several carbonic anhydrase inhibitors on urinary excretion of citrate by humans was studied.

Acetazolamide (250 mg. q6h), methazolamide (100 mg. q8h) or dichlorphenamide (50 mg. q6h or 100 mg. q8h) were approximately equally effective in causing a marked decrease in urinary excretion of citrate. Citrate excretion was decreased by approximately 80 percent after 48 hours of therapy. This low level of citrate excretion persisted at least one week after discontinuing the chronic administration of one of these carbonic anhydrase inhibitors (acetazolamide).

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ULTRASTRUCTURE OF PIGMENT GRANULES OF RETINAL EPITHELIUM*

II. Dog, fish, frog, monkey, mouse, and pig

Yoshiaki Taniguchi, M.D.
Fukuoka, Japan

This report is to compare the electron-microscope findings of the retinal pigment granules of the following vertebrates (dog, fish, frog, monkey, mouse, and pig) with those of the cow eye described in Part I[1] of this study. In general, the features have been strikingly similar in all these species.

Materials and Methods

The experimental animals used in this study were dog, frog (Rana clamitans), monkey, mouse, pig, and sunfish (Lepomis gibbosus), and the methods of tissue preparation employed were those previously reported in Part I. The eyes were light adapted and obtained fresh. Hypotonic saline (0.4 and 0.6 percent) and horse serum (60 and 80 percent with distilled water as diluent) were used for cytolysis.

When hypotonic saline was used, a small quantity of the granules was drawn up and put into distilled water in another tube to wash away the sodium chloride crystals. Occasionally, distilled water was dropped on the dried grid to dissolve the crystals.

In order to demonstrate the internal structure of the granules, part of the suspension was treated with 80-percent ethyl alcohol and part treated with four-percent chloramin-T to observe the effect of a clearing agent.

The RCA electron microscope type EMU-2 was employed throughout.

Observations on the Pigment Granules

Form and size

The pigment granules in the several vertebrate eyes studied were polymorphous (figs. 1, 2, 3, 4, 5, and 6). They were of three types: cigar-shaped, egg-shaped and spherical. In addition, curved or crescent forms

Fig. 1 (Taniguchi). The pigment granules of the monkey eye (Platinum shadowing; ×18,000.)

of these were seen; there were other shapes of the granules, also, which were grouped together as irregular, but the percentage of these shapes was small.

The cigar-shaped granules of the fish had rounded ends, and some of them were quite long (figs. 6 and 17).

After examining five or more cigar-shaped granules in each species, the following range of the lengths were found: Dog, 0.8-2.4 μ; fish, 1.0-3.3 μ; frog, 1.0-3.0 μ; monkey, 0.9-2.8 μ; mouse, 0.7-2.0 μ; pig, 0.6-2.8 μ.

The range of the diameters in the spherical forms were: Dog, 0.3-1.0 μ; fish, 0.3-0.7

* From the Department of Ophthalmology, Indiana University School of Medicine. This study was supported by a grant from the Knights Templar Eye Foundation. Reprint requests should be addressed to the Department of Ophthalmology, 1100 West Michigan Street, Indianapolis 7, Indiana.

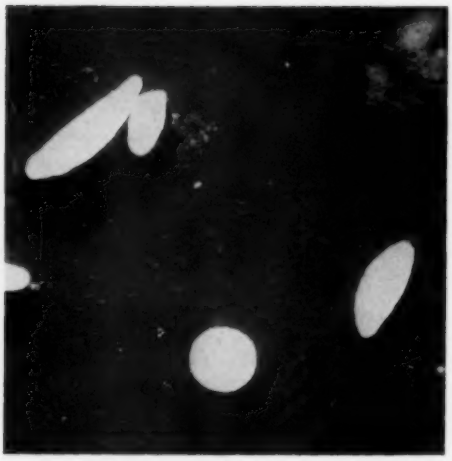

Fig. 2 (Taniguchi). The pigment granules of the dog eye. (Platinum shadowing; ×10,000.)

μ; frog, 0.3-1.2 μ; monkey, 0.3-0.6 μ; mouse, 0.2-0.9 μ; pig, 0.2-0.6 μ.

Surface and internal structure

After treatment with either four-percent chloramin-T or 80-percent ethyl alcohol, the pigment granules shrank and developed irregular projections. Figure 7 shows the pigment granules of the dog eye with many projections seen at larger magnifications. In some cases the granules split into a large number of tiny microgranules. Figure 8 reveals the result of treating monkey pigment granules with four-percent chloramin-T. It was assumed that the granules were disrupted by the agent and many microgranules released.

The granules from the pig (fig. 9) and

Fig. 3 (Taniguchi). The pigment granules of the pig eye. (Platinum shadowing; ×8,000.)

Fig. 4 (Taniguchi). The pigment granules of the mouse eye. (Platinum shadowing; ×11,000.)

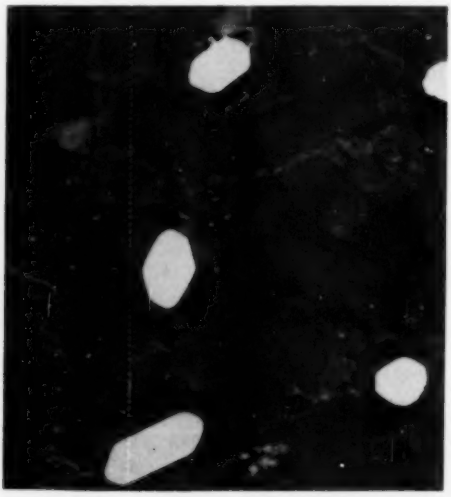

Fig. 5 (Taniguchi). The pigment granules of the frog eye. (Platinum shadowing; ×9,000.)

Fig. 6. (Taniguchi). The pigment granules of the fish eye. (Platinum shadowing; ×18,000.)

from the mouse (fig. 10) were treated with 80-percent alcohol. These microgranules appeared to be contained in a thin membranous sac which seemed to be destroyed by the alcohol, allowing the microgranules to escape. The shape of the microgranules appeared in all instances to be that of the parent granules.

Figure 11 suggests the internal structure of the frog pigment granule; it seemed to consist of many tiny egg-shaped microgranules. The membrane was partially destroyed, and some microgranules apparently separated from their parent granule.

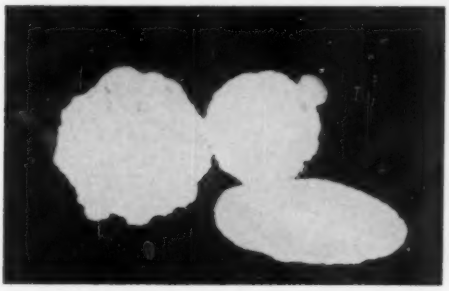

Fig. 7 (Taniguchi). The pigment granules of the dog eye, with many projections. (×29,000.)

Fig. 8 (Taniguchi). The microgranules of the monkey eye treated with chloramin. (×18,000.)

Filamentous processes

In each of the species treated with hypotonic saline or horse serum, thin filamentous

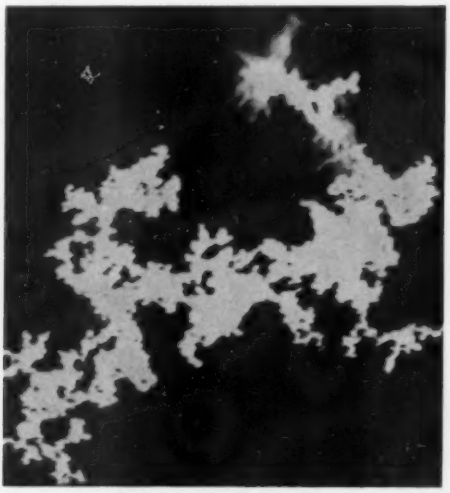

Fig. 9 (Taniguchi). The microgranules of the pig eye treated with 80-percent alcohol. (×28,000.)

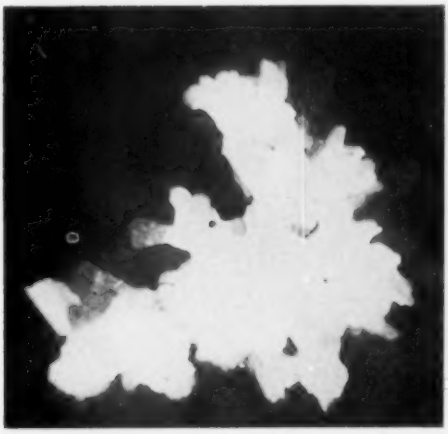

Fig. 10 (Taniguchi). The pigment granules of the mouse eye treated with 80-percent ethyl alcohol. (×42,000.)

processes were found on each of its extremities (figs. 12, 13, 14, 15, 16, and 17).

According to the observations here, it was only the cigar-shaped granules which had filaments at both extremities; whereas, the spherical-shaped granules had no filaments at all. The filament attached to the cigar-shaped granules ordinarily appeared to connect two granules and to run parallel to the major axis of the granule, and it was obliquely striated (figs. 13, 14, and 16). Sometimes the filament could be seen to consist of two thinner strands (figs. 12, 14, and 16).

The filamentous prolongations varied

Fig. 11 (Taniguchi). The pigment granule of the frog eye treated with 80-percent ethyl alcohol. It consisted of numerous egg-shaped microgranules. (×37,000.)

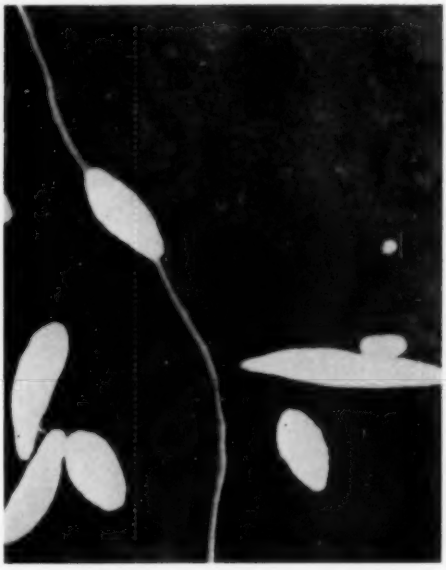

Fig. 12 (Taniguchi). The filamentous process of the pigment granule of the monkey eye. (Platinum shadowing; ×19,000.)

from one to eight times the length of the pigment granules but were usually about four or five times granule length. The width of the filaments varied from about 50 to 90 mμ, but some of them reached 120 mμ.

The connection of the filament to the granule appeared tenuous, so that it could separate from the granule.

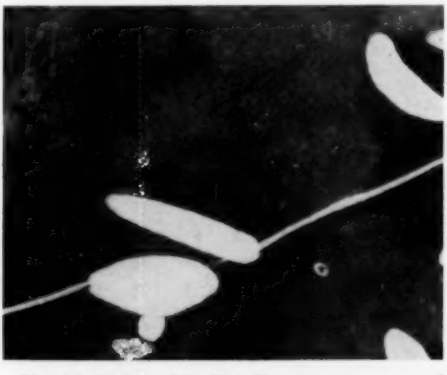

Fig. 13 (Taniguchi). The filamentous process of the pigment granule of the monkey eye. (Platinum shadowing; ×18,000.)

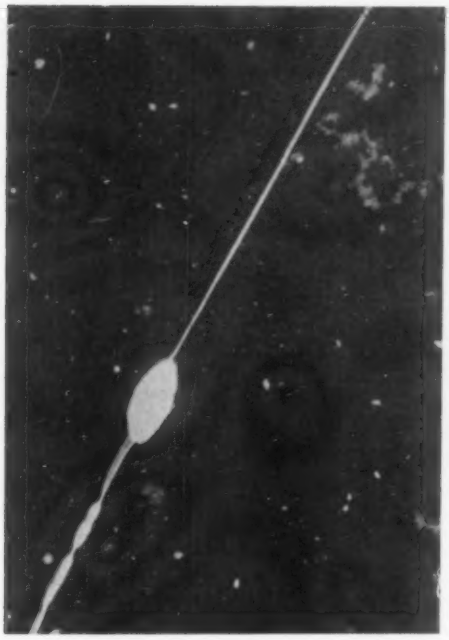

Fig. 14 (Taniguchi). The filamentous process of the pigment granule of the dog eye. (×10,000.)

Fig. 16 (Taniguchi). The filamentous process of the pigment granule of the frog eye. (Platinum shadowing; ×15,000.)

Discussion

Sebruyns was the first to study the pigment granules in the retina of the ox with the electron microscope.[2] He stated that each granule had a filamentous process at one of

Fig. 15 (Taniguchi). The filamentous process of the granule of the mouse eye (Platinum shadowing; ×11,000.)

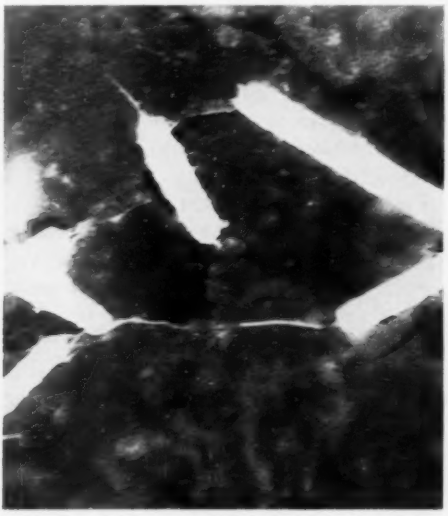

Fig. 17 (Taniguchi). The filamentous process of the pigment granule of the fish eye. (Platinum shadowing; ×17,000.)

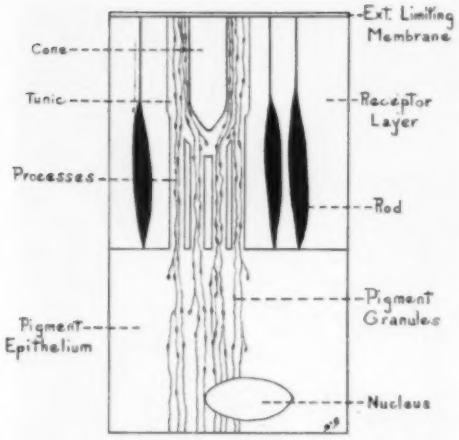

Fig. 18 (Taniguchi). The relation between the pigment granules and the retinal epithelial cell.

its extremities, that the expansion and contraction of this filament caused the migration of the pigment granules, and that the pigment granule was composed of several hundred microgranules. Subsequently Binder and Orth[3] (1953), in their studies of the human pigment granules, François, Rabey and Vandermeerssche[4] (1953) in their observations of the human, cow, frog, and carp, and Kinugasa[5] (1953) in his studies of the cow, and Lion, Maertens, and Vandermeerssche[6] (1957) in their observations of the monkey, pig, and guinea pig failed to observe the presence of filaments or any internal structure.

Binder and Orth found two types of pigment granules in the human eye, the first type was spindle-shaped with an irregular boundary, the second one spherical with small grains on its surface; they felt that these observations suggested an internal structure of the pigment granules. Later, Takeuchi[7] (1956) while studying the pigment granules of the human eye observed no internal structure but did observe a filament.

Already described in Part I[1] of this study were the pigment granules of the cow eye and their internal structure and filamentous processes at both ends of some of the granules. In the present study, almost identical microgranules and filamentous processes in six additional species were observed (dog, fish, frog, monkey mouse, and pig).

François, et al.[4] (1953) said that the pigment granules were rapidly destroyed by chloramin, and Heydenreich[8] (1957) stated that the pigment granules were destroyed in 20 to 40 hours by four-percent chloramin.

In this study, it was observed that monkey pigment granules were destroyed by four-percent chloramin and broken into many microgranules, but the details of the internal structure were not observed.

The internal structure of the granules of the retinal pigment epithelium was previously observed only by Sebruyns[2] and Iwaki,[9] but their observations were somewhat equivocal.

In the studies of Birbeck, et al.[10] in the pigment granules of human hair it was found that many granules broke into irregular small particles, some of which revealed an internal structure of parallel lamellae.

It has shown in all the vertebrates studied, including monkey and man,[11, 12] but especially in amphibians and fishes, that when the dark-adapted eye is illuminated, the pigment granules in the pigment epithelium migrate inwardly.

I agree with Sebruyns that the filaments we have observed may be closely related to the migration of the pigment granules.

According to my observations, cigar-shaped pigment granules have a filamentous process, which connects two granules at both extremities of the granule. It is possible that the pigment granules may keep their proper position by means of torsion and perhaps by a connection of the filaments with both the external and internal extremities of the cell.

Figure 18 diagrams the hypothetical arrangement of pigment granules and their filaments with a pigment epithelial cell of the vertebrate retina.

Upon exposure to light, somehow, perhaps through photochemical changes, the filament on the inner side may be made to become more twisted so that the granule moves inward toward the more twisted filament. When dark adapted, the filament on the inner side may become less twisted, so that the migrated granules can move back to their original positions.

Conclusion

An electron-microscope study of the retinal pigment granules of several vertebrate eyes (dog, fish, frog, monkey, mouse, and pig) produced the following observations:

1. The pigment granules revealed a number of forms, usually cigar-shaped, but also egg-shaped and spherical.

2. These granules were composed of numerous microgranules with the same shape as the parent granules.

3. The cigar-shaped pigment granules had filamentous processes at both extremities, and these filaments averaged four to five times the length of the granule itself.

An hypothesis concerned with a partial explanation of the migration of pigment granules in the retinal epithelial cells is suggested.

Acknowledgment

I wish to acknowledge the kind assistance of L. W. Freeman, M.D., Luis Lorenz Estella, and R. E. Smith in the collection of animal eyes and the help of Fred M. Wilson, M.D., and T. F. Schlaegel, Jr., M.D., in the preparation of the paper.

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SECRETION OF INORGANIC PHOSPHORUS IN TEARS*

Joseph Balík, M.D.
Prague, Czechoslovakia

The level of inorganic phosphates has not yet been determined. Magaard was not able to prove them in a qualitative examination of the tear fluid, although Frerichs and Arlt and Lerch summarize the value of the salt components, as well as the phosphates, sodium, potassium, and ammonia; Frerichs included the chlorides, Arlt and Lerch determined them separately. deRoetth mentions phosphates but Ridley in his discussion of the analytical survey of Brown says nothing

* From the First Ophthalmic Clinic of the Charles University. Director: Prof. Dr. E. Dienstbier.

to prove examination of phosphates in the tear fluid.

Phosphates exist in body fluids as soluble primary phosphates and as alkali phosphates. In addition they are components of such solid structures as bones, teeth, muscles, and so forth. Finally they are components of organic substances in which they have their particular importance. Phosphates dissolved in the body fluids may form a buffer system, which is of less importance than the system of proteins or bicarbonates (Hamsík, Šantavý). It seemed probable that they could be found in tears but to prove this posed technical difficulties. Proof of their presence in tears would have been only relative, for only minute quantities were available for investigation, since only minute quantities are present in the conjunctival sac during normal tearing.

Examination and Observations

The usual technique of taking of tears was used. To avoid errors due to very small amounts of tears, tear fluid was taken from both eyes and the heavier sample was always examined. The quantities of tear fluid were sufficient for the examination and repeated collections were avoided so as not to change the correlations and results. A group of 30 normal persons (14 men between 18 and 75 years of age and 16 women between 15 and 82 years of age) were examined. Blood samples from the elbow vein were collected at the same time as the tears.

The technique of Lowry and Lopez, modified for present needs, was used for the examination; the principle of this method is the development of a blue color of phosphomolybdate acid, as determined by the spectrophotometer at 700 mμ. These authors say that it is possible by their method to determine inorganic phosphorus in the presence of labile phosphate esters. Reagents were:

1. 5.0-percent solution of trichloracetic acid
2. 0.1 N sodium acetate
3. 1.0-percent solution of ascorbic acid
4. 1.0-percent solution of ammonium molybdate in 0.05 N sulfuric acid.

Tear examination

Whatman No. 1 chromatographic paper is soaked with tears. This paper which does not contain any phosphorus, is inserted into 1.0 ml. of trichloracetic acid. Special deproteination is not necessary because the solution will not become turbid, probably because of the small quantity of mucin which adheres to the paper. After 10 minutes, 4.0 ml. of sodium acetate are added. After another 10 minutes, the paper is extracted and pressed out on the wall. Any error developing during this treatment would be slight with regard to the total volume because a paper absolutely saturated during taking of the tear fluid contains not even 100 μl. of fluid. Next 0.5 ml. of ascorbic acid and 0.5 ml. of ammonium molybdate are added and at the 10th minute are studied colorimetrically.

Blood examination

One ml. of serum is mixed with 9.0 ml. of trichloracetic acid. After standing for 10 minutes, it is centrifugated for 10 minutes. Eight ml. of sodium acetate, 1.0 ml. of ascorbic acid, and 1.0 ml. of ammonium molybdate are added to the 2.0 ml. of clear supernatant and colorimetrically determined under the same conditions as for tears.

In both examinations (tears and blood) control samples containing the same reagents without phosphorus were colorimetrically determined in the same manner at the 10th minute and compared with the distilled water, their color being subtracted from the color of the unknown samples.

Calibration. 0.439 gr. KH_2PO_4 is dissolved in 100 ml. of distilled water (1.0 ml. contains 1.0 mg. of P), 0.1 ml. of this solution is adjusted to 100 ml. with trichloracetic acid (1.0 ml. contains 5.0 μg. of P). Then 0.5, 1.0, 1.5, and 2.0 ml. of the last solution are adjusted to 10 ml. with acetate and 1.0 ml. of ascorbic acid and 1.0 ml. of molybdate solution are added. The control sample contains, instead of the phosphorus solution, 2.0 ml. of trichloracetic acid. The color is investigated in the same manner as the samples of

TABLE 1

SURVEY OF RESULTS

Name	Age (yr.)	Tears		Blood P-level (mg.%)	Fs
		Collected (mg.)	P-level µg./mg.		
B. J.	42	18	0.132	4.38	3.02
K. A.	46	29	0.082	2.97	2.77
K. B.	42	12	0.185	4.37	4.25
C. J.	33	88	0.035	4.65	0.77
Z. M.	48	8	0.284	4.33	6.54
E. M.	78	24	0.114	3.40	3.36
S. M.	71	11	0.213	3.95	5.93
T. F.	24	47	0.067	3.95	1.69
K. B.	58	13	0.111	2.97	3.75
V. A.	21	13	0.141	4.02	3.52
S. V.	15	42	0.072	5.00	1.43
S. J.	18	47	0.055	4.30	1.27
M. S.	30	45	0.034	3.52	0.97
S. A.	30	11	0.125	3.54	3.53
N. V.	74	31	0.101	5.98	1.69
H. F.	65	11	0.302	5.62	5.37
V. M.	64	31	0.100	5.31	1.88
H. E.	42	50	0.068	6.10	2.06
J. E.	37	85	0.040	4.38	0.90
R. V.	23	83	0.034	4.38	0.77
M. B.	28	67	0.034	3.95	0.87
W. H.	18	76	0.030	4.68	0.65
S. A.	53	92	0.036	3.40	1.05
V. J.	26	5	0.320	3.40	9.40
B. B.	21	7	0.274	4.18	6.55
S. A.	61	23	0.102	4.65	2.20
N. M.	46	21	0.088	3.87	2.26
S. A.	65	22	0.094	3.16	2.98
H. M.	70	7	0.313	3.67	8.53
P. B.	30	74	0.032	3.87	0.82

tears and blood. The mean error of the determination averages around three percent.

Calculation of tears. The quantity of phosphorus per µg., calculated from the calibration equation, is divided by two (the reaction takes half the quantity). The result indicates the quantity of inorganic phosphorus in each sample of tear fluid. Dividing by the weight of tears in mg. the concentration of phosphorus in 1.0 mg. of tear fluid is obtained.

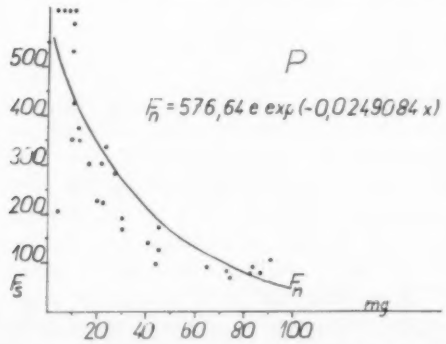

Fig. 1 (Balík). Relationship of secretory factor (Fs) to the mg. of tears.

Blood. The quantity calculated in mg. is multiplied by 500 and the concentration of phosphorus in mg. percent is obtained. The secretory factor (Fs) is calculated from these two values. A survey of results is given in Table 1. Table 2 surveys the calculated relationships. The relation of the secretory factor (Fs) to the mg. of tears is shown graphically in Figure 1.

DISCUSSION

The first mean value confirms the principle which had to be used in the investigation in order to avoid as far as possible mistakes in examining the very minute samples. The

TABLE 2

CALCULATED RELATIONSHIPS

N	30.00	
Average of tearing (mg.)	37.43	s=29.05
Average quantity of P in the tears (μg.)	2.49	s= 0.593
Average level of P in serum (mg.%)	4.213	s= 0.817
Average concentration of P of tears (mg.)	0.1206	s= 0.0928
Average of secretory factor (Fs)	3.02	
Correlation of total quantity of P in tears and blood level of P	0.59	t= 3.867 for 28 degrees of freedom
Correlation of the concentration of P in tears and blood level of P	0.034	
Concentration dependence of P in tears on tearing/η^* = log conc.10^3		
$\eta^* = 2.3612 - 0.0105755 \times$		
b= −0.0105755		
t= 20.62 for 28 degrees of freedom		
Dependence of the secretory factor on tearing/θ − log Fs. 10^2		
$\theta^* = 2.7609 - 0.01081757 \times$		
b=0.0108175F		
t=12.08 for 28 degrees of freedom		

higher average, however, differs little from the mean value of the secretory factor, which fluctuates around 30 mg., showing that the level of inorganic phosphorus in tears is probably three times higher than in blood. This is an interesting observation. The correlation of the total quantity of phosphorus in the conjunctival sac to the phosphorus level in blood is likewise interesting. It shows that about 60 percent of it probably depends on the blood level. The second source of phosphorus—the conjunctival goblet cells—could account for the remainder. As far as the concentration of phosphorus in tear fluid is concerned, this rather remarkable correlation could not be proved but differences were so slight that further tests seemed unnecessary. The concentration of phosphorus in tear fluid seems not, therefore, to depend on its blood level. Logarithmic and exponential analyses show, moreover, that the concentration falls with increased tearing.

The secretory factor behaves similarly. Its value is not constant either, but changes with a change in the amount of tear fluid. The decrease of both values can be statistically verified.

Examination of phosphates in the tear fluid showed the mechanism of secretion compared to chlorides. Both are anions and both seem to be secreted into tears in the same manner. However, a comparison seems to provide convincing evidence that, with chlorides, the secretory factor increases from the first tearing, perhaps because of increased function of the conjunctival goblet cells. In phosphates quite the reverse seems true. Their concentration in tears falls as the secretion increases. The importance of phosphates as a buffer system in tears may be slight, as in serum, because their quantity is meager as compared to proteins. Phosphates could be used to adjust the pH of eyedrops. A slight decrease in concentration of phosphorus could be related to the consumption of these compounds in the production of the materials necessary as a source of energy for cell/secretory/activity.

SUMMARY

Colorimetric examination of tear samples from 30 normal persons (method of Lowry and Lopez) showed that tears contain inorganic phosphates in the amount of about 2.49 μg. in the average tearing of 37 mg. The concentration of phosphorus in 1.0 mg. of tears does not depend on the blood level but on the change of tearing. The secretory factor (Fs), showing that the concentration of inorganic phosphorus in tears is about three times higher in average tearing, gives simi-

lar results. The two values (concentration and secretory factor) have similar exponential correlation in increased tearing. This differs fundamentally from the secretion of chlorides into tears; in increased tearing their secretory factors increase slowly and linearly.

Jerevanská 8/702 (13) Vršovice.

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CONGENITAL APHAKIA*

J. Reimer Wolter, M.D., and Manos A. Petrohelos, M.D.
Ann Arbor, Michigan

Congenital aphakia is an extremely rare anomaly which is usually found in eyes with other serious congenital defects. Most of the cases of this rare anomaly in the literature are clinical observations without histologic confirmation. The reported case represents a complete clinical and histopathologic study of an eye with congenital aphakia.

Case history

This 37-year-old white man was first seen on April 25, 1957. He gave a history of having been born with his right eye blind and much smaller than normal. There was no history of any eye trauma. There was no other anomaly known in his family and there was no parental consanguinity. The patient had been a full-term baby.

The eye examination revealed his vision to be: O.D., blindness; O.S., *20/20*, with −2.0D. sph. ⌒ +0.25D. cyl. ax. 90°. No nystagmus was seen. The right eye appeared microphthalmic and the horizontal corneal diameter was 8.5 mm. The globe was white, conjunctiva and sclera were normal. The cornea of the right eye exhibited a white central scar in the subepithelial layers of the stroma. This scar extended horizontally toward the limbus and thus simulated a band keratopathy. The anterior chamber was deep. The pupil was central. No flare or cells were seen. The iris was atrophic. A whitish membrane was seen in the place of the lens. It was not possible to see into the posterior chamber or to visualize the fundus. However, the globe could be well transilluminated. The left eye was essentially normal. The intraocular pressure was normal in the left eye. Tonometer measurements in the right eye indicated an increased intraocular pressure. However it was felt that the tonometer was of no value in this microphthalmic eye with an old degenerative central scar in a small and thickened cornea. The intraocular pressure appeared normal at finger palpation.

The patient expressed the desire to have the right eye removed for cosmetic reasons. An enucleation was performed December 18, 1958.

Histologic examination

Method

The eye was cut in two halves both of which were imbedded in paraffin and cut in serial sections. These sections were stained with hematoxylin eosin.

All pictures of this paper are unretouched photomicrographs.

Results

The macroscopic examination revealed the eye to be of normal shape and to measure 16 by 15 by 15 mm. The horizontal corneal diameter was 8.5 mm. After opening the globe the anterior chamber was found to be

* From the Department of Ophthalmic Surgery and from the Laboratory of Neuropathology of the University of Michigan Medical Center. Supported by Grants No. 2B-5163 (C) and B-475-C5 of the United States Department of Public Health Education and Welfare.

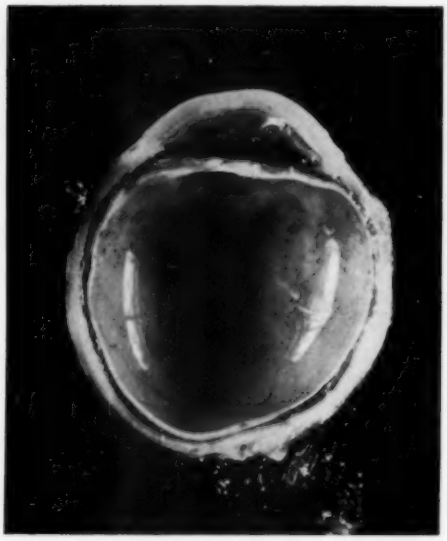

Fig. 1 (Wolter and Petrohelos). Macroscopic view of one half of the eye. The thickened cornea, the deep chamber, and the pupillary membrane are clearly visible.

of about normal depth (fig. 1). No lens was seen and a dense white membrane was found in the place of the lens. Ciliary processes and peripheral retina were pulled toward this membrane. The posterior chamber was filled with a clear fluid of waterlike consistency.

The microscopic examination of the histologic slides showed a multitude of interesting pathologic alterations. The corneal epithelium was continuous but of irregular thickness and architecture. It showed several areas of separation from the underlying structures (fig. 2). Bowman's membrane was absent except for several small isolated areas. Extensive superficial scarring of the stroma was found. This exhibited many areas of calcification. The stroma as a whole was thickened. The corneal endothelium was somewhat atrophic. The iris showed a very advanced stage of iridoschisis[1] (figs. 3 and 4). The pigment epithelium and the sphincter and dilator muscles were rather well preserved but the iris stroma was extremely loose and atrophic. The filtration angle appeared well developed and open (fig. 5). The trabecular meshwork was of normal architecture. Many cellular nuclei were seen in the trabeculae and in Schlemm's canal. A dense scarlike connective tissue membrane with many blood vessels in it was found in the place of the lens (fig. 2). This membrane included the inner ends of most ciliary processes. The latter were very much elongated (figs. 2 and 6) and somewhat atrophic. The ciliary body as a whole was small and atrophic (fig. 2). Posteriorly the peripheral retina was incorporated in the pupillary membrane and the whole peripheral and intermediate retina was pulled forward (figs. 2 and 7). It is important to emphasize that the membrane found in the place of the lens was composed of dense connective tissue and many small blood vessels (fig. 7). No part of the lens, not even a piece of lens capsule, could be found in our serial sections.

The retina at the posterior pole was about normal (fig. 8). Cystic degeneration and atrophy of all layers including that of the rods and cones was found in the intermediate retina (fig. 9). Advanced atrophy and pigment deposition around the blood vessels was seen in the peripheral retina (fig. 10). An occluded persistent hyaloid artery was seen at the disc (fig. 11). It extended into the posterior chamber but did not reach the pupillary membrane (figs. 2, 12-a and b). It is very interesting that the wall of Cloquet's canal could be very well demonstrated in the slides (fig. 12-b). No other structures of secondary vitreous were seen. The choroid was somewhat thin and atrophic. It showed extensive formation of drusen (colloid bodies) in its periphery. The optic nerve appeared about normal. Both central vessels were found to be open. The sclera appeared somewhat thickened but was of normal structure.

The pathologic diagnosis was microphthalmos with old band keratopathy, iridoschisis, congenital aphakia, persistence of the tunica vasculosa lentis and formation of a scarlike

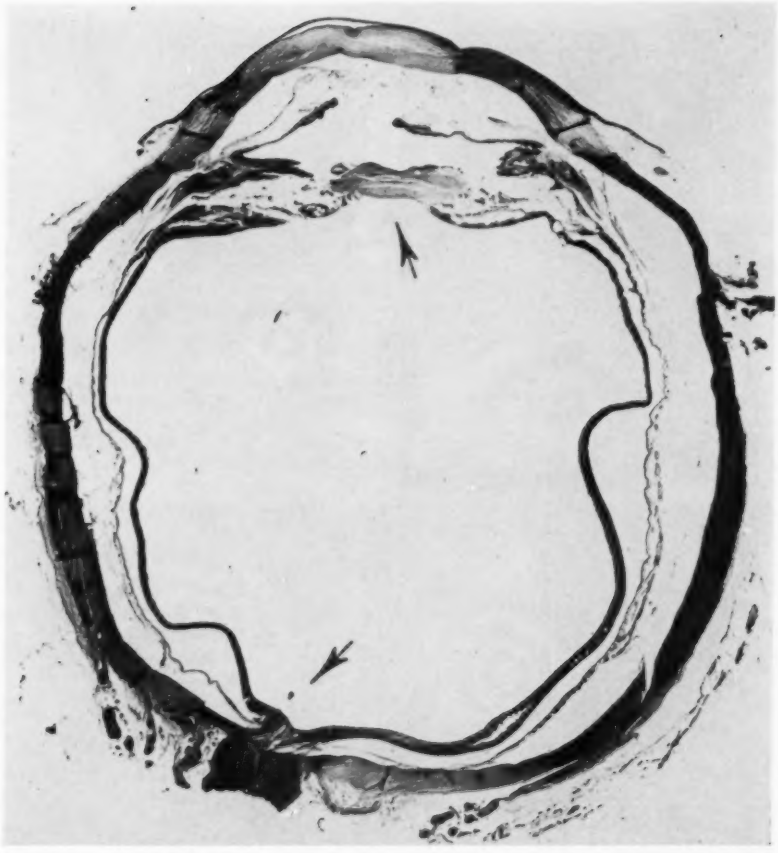

Fig. 2 (Wolter and Petrohelos). Low-power view of a histologic section through the eye. Arrows point to the membrane and to the persistent hyaloid artery. Ciliary processes and peripheral retina are incorporated in the pupillary membrane and are pulled into it. (Hematoxylin-eosin.)

vascular membrane, persistence of the posterior part of the hyaloid artery, and secondary retinal degeneration.

Comment

This is a very unusual eye. It presents many of the features of a somewhat more common congenital anomaly: that of persistent hyperplastic vitreous.* This entity typically exhibits microphthalmos, malformation of the filtration angle, cataract and kidney-shape of lens, persistent tunica vasculosa lentis, elongation of the ciliary processes, advancement of the peripheral retina, persistence of the hyaloid artery, lack of normal vitreous, fibrous filaments in the posterior chamber and a multitude of pathologic changes of the retina.[2-5] The outstanding feature of this case, however, is that there was no lens and not even a piece of lens capsule found in or on the pupillary membrane. This fact allows for classification of this case into the group of the extremely

* Reese suggested this simpler term in a personal communication instead of "persistent hyperplastic primary vitreous."

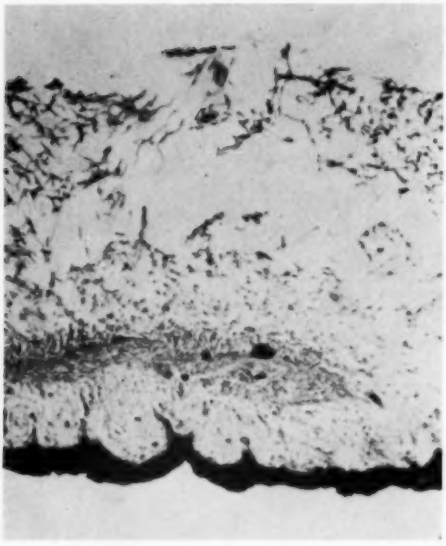

Fig. 3 (Wolter and Petrohelos). An area of the iris close to the pupil. The pigment epithelium is well preserved, the sphincter muscle is also of about normal structure. The stroma is very atrophic and loose. (Hematoxylin-eosin.)

Fig. 4 (Wolter and Petrohelos). Another area of the iris that shows advanced iridoschisis. (Hematoxylin-eosin.)

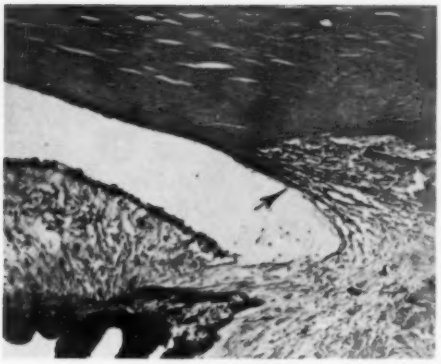

Fig. 5 (Wolter and Petrohelos). High-power view of the normal chamber angle. (Hematoxylin-eosin.)

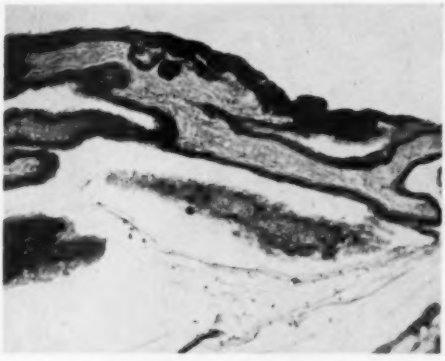

Fig. 6 (Wolter and Petrohelos). Elongated ciliary processes. (Hematoxylin-eosin.)

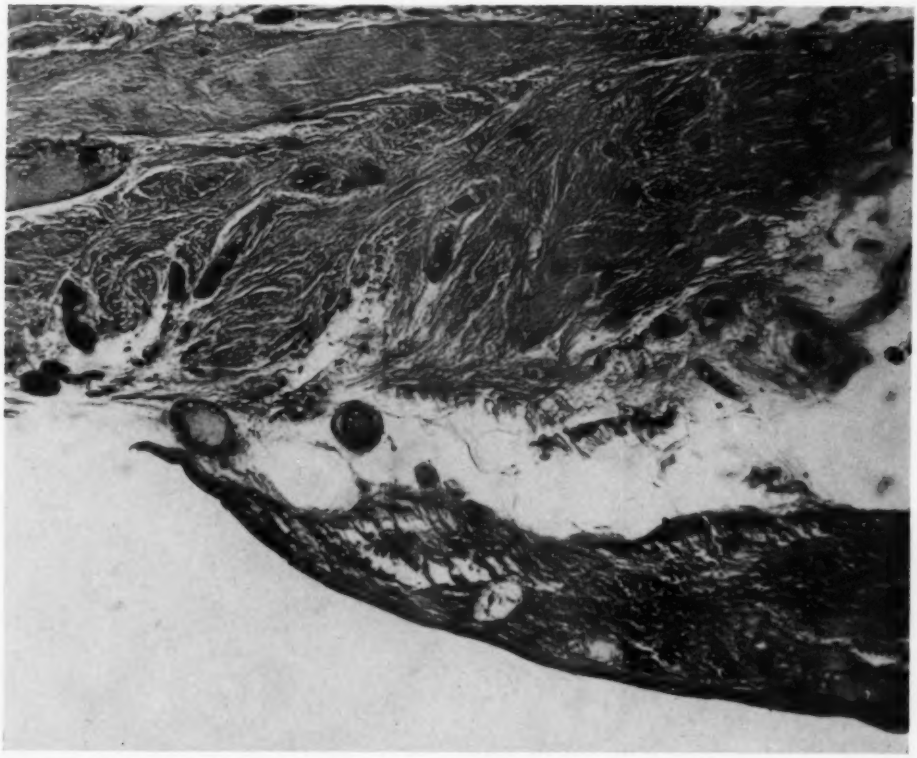

Fig. 7 (Wolter and Petrohelos). Part of the pupillary membrane (persistent tunica vasculosa lentis) with many small blood vessels in it. The attachment of the peripheral retina is seen in this area. (Hematoxylin-eosin.)

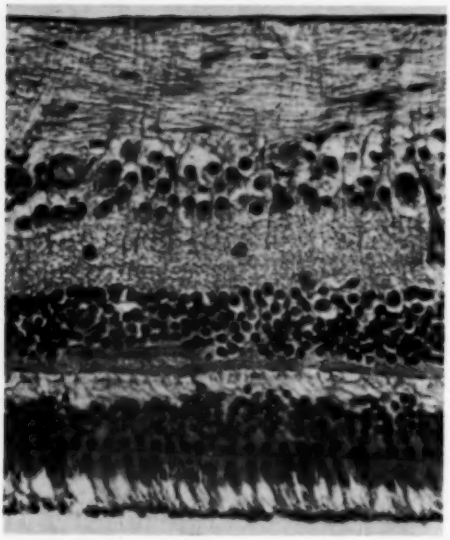

Fig. 8 (Wolter and Petrohelos). Retina of the posterior pole of this eye looks perfectly normal. (Hematoxylin-eosin.)

rare anomaly of congenital aphakia. As a matter of fact, it appears that this is the first case in the literature in which absence of a lens could be proven histologically in an adult eye.

The first report of a case of congenital aphakia is that of Baker[6] in 1887. A 16-year-old boy was clinically found to have no lens or capsule remnants in either eye. In 1898, Rabl[7] observed a case of unilateral aphakia in an amblyostoma embryo. The condition was associated with general failure of ectodermal structures on the same side of the head and the central nervous system. In 1900, Tiffany[8] reported the clinical observation of two brothers with congenital aphakia.

Another clinical report is that of Cherry-holmes[9] in 1902. This was the case of an eight-year-old boy with bilateral microphthalmos, aphakia and nystagmus. In 1905, Gratiot[10] reported a 30-year-old man with a history of poor vision since birth. This patient exhibited iridodenesis, nystagmus, and displacement of the pupils with aphakia in both eyes.

Mohr[11] described a case of congenital aphakia in a pig, associated with several other deformations. Additional clinical observations of congenital aphakia were reported in 1915 by Adams,[12] Hardey,[13] Risley,[14] and Sherer.[15]

Mann,[16] in 1921, described an unique case in a human fetus of 13-mm. length that failed to show a lens in either eye. Weve[17] reported an interesting clinical observation of unilateral aphakia in a 16-year-old boy. The aphakia in this case was associated with per-

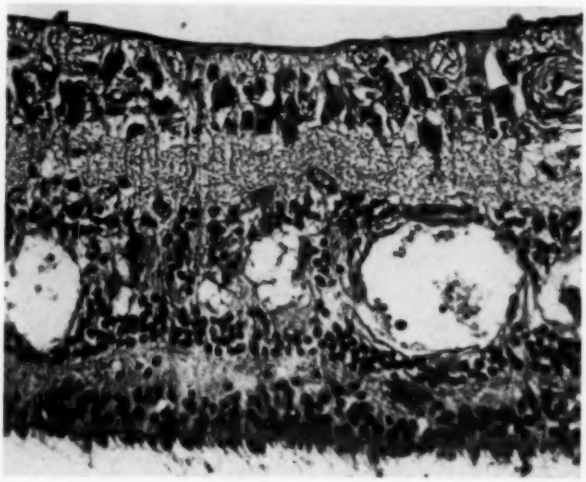

Fig. 9 (Wolter and Petrohelos). The intermediate retina shows extensive cystoid degeneration, loss of the nerve-fiber layer and changes of the rods and cones. (Hematoxylin-eosin.)

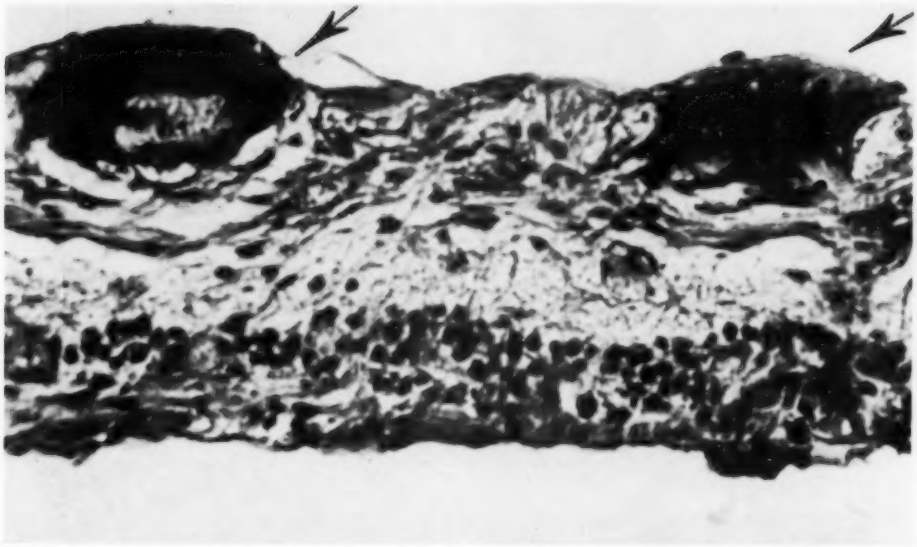

Fig. 10 (Wolter and Petrohelos). The peripheral retina is thin and atrophic. Pigment is deposited around the retinal blood vessels (arrows). (Hematoxylin-eosin.)

sistent hyaloid artery as a partial retinal fold. The involved eye was amblyopic. Saltzman and Light[15] reported, in 1951, the most recent clinical observation of a case of congenital aphakia associated with slit pupil.

This short review of cases reported by many well-known ophthalmologists leaves little doubt that the entity of congenital aphakia really exists. It also shows that eyes without lenses obviously may develop to about their normal shape and size. However, microphthalmos seems to be rather common in these cases. A persistent hyaloid artery had also already been reported in one of these cases by an earlier author.[17] The present case seems different from the earlier clinical ob-

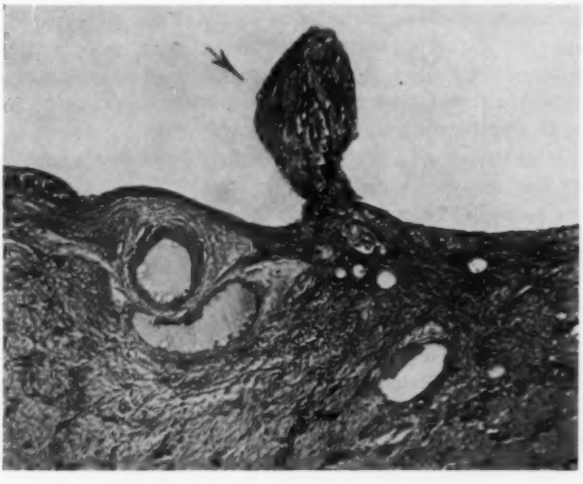

Fig. 11 (Wolter and Petrohelos). Longitudinal section through the optic nerve. The arrow points to the occluded persistent hyaloid artery as it comes off the optic nerve head. (Hematoxylin-eosin.)

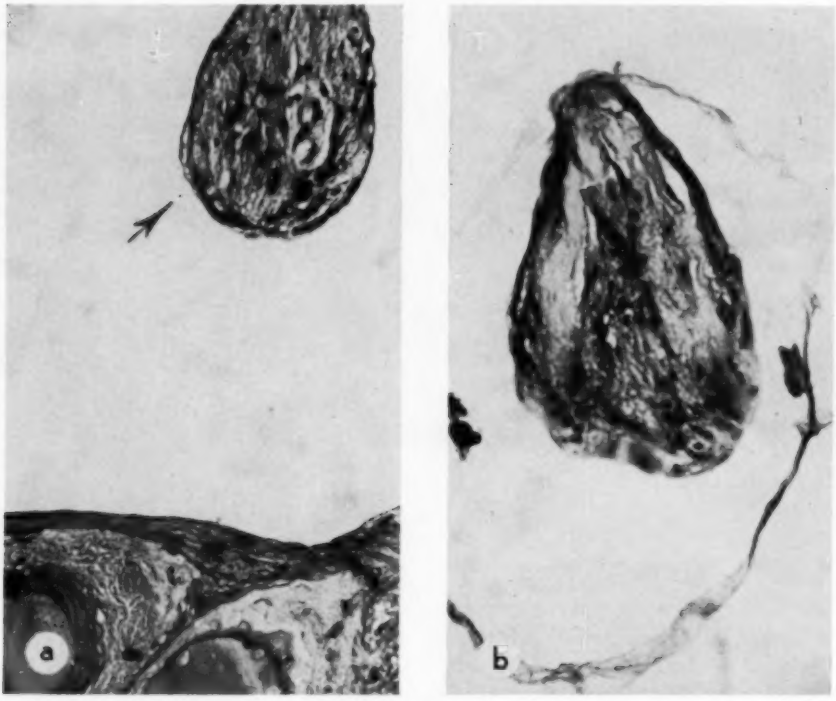

Fig. 12 (Wolter and Petrohelos). (a) Another picture of the occluded hyaloid artery in the vitreous (arrow). The optic nerve head is seen below. (Hematoxylin-eosin.) (b) The occluded persistent hyaloid artery in the posterior chamber surrounded by the thin wall of Cloquet's canal. (Hematoxylin-eosin.)

servations in so far as our case showed a dense membrane instead of the lens. It was therefore impossible to make the diagnosis in our case just by clinical examination. It is important to emphasize that the present case appears to be closely related to the condition known as persistent hyperplastic vitreous.

The pathologic examination did not verify the statement of the patient that he was totally blind in his right eye. The retina at the posterior pole and the optic nerve appeared about normal and the patient should have been able to see at least light with this eye.

We consider the fact of the existence of a well-developed wall of the canal of Cloquet in this case as evidence that a secondary vitreous must have been present. This probably became liquefied as it often does in degenerative conditions of the eye. Other degenerative changes were seen in the cornea, the iris, and the retina of this eye. It seems surprising to us that an eye of normal shape and relatively normal size could develop without the presence of a lens. Moreover, it seems surprising that we found a persistent tunica vasculosa lentis in the total absence of a lens. This observation indicated that an eye without a lens may go on in its development with relatively little disturbance. Our case gives no answer, however, to the question at which stage of ocular development the disturbance of the formation of the lens occurred and whether the lens was primarily absent or not.

Summary

The clinical and histologic study of an

eye with congenital aphakia in a 37-year-old patient is reported. The eye showed most of the changes of the congenital anomaly known as persistent hyperplastic vitreous with the additional total absence of the lens.

University Medical Center.

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OCULAR MANIFESTATIONS OF NARCOLEPSY*

William P. Keefe, M.D., Robert E. Yoss, M.D., Theodore G. Martens, M.D., and David D. Daly, M.D.

Rochester, Minnesota

Introduction

The narcoleptic syndrome has long interested neurologists; however, the ocular manifestations of the syndrome are relatively unfamiliar to ophthalmologists. Ocular disturbances occur frequently in narcoleptic persons, and in many such patients they constitute the presenting symptom. Among the prominent complaints are intermittent diplopia, blurring of vision, difficulty with reading and ptosis.

For an understanding of these complaints, a brief review of the nature of the narcoleptic syndrome[1] may be helpful. The narcoleptic tetrad consists of four symptoms: (1) excessive sleepiness or narcolepsy, (2) cataplexy, attacks of muscular weakness induced with emotion, (3) sleep paralysis, and (4) hypnagogic hallucinations. In the past the narcoleptic syndrome has been regarded as a neurologic curiosity. In recent years a better understanding of the basic disorder has led to recognition of it with increasing frequency. The availability of effective analeptic agents[2] reemphasizes the importance of early recognition of the disease.

The universal member-symptom of the tetrad is excessive and abnormal sleepiness. The insidious appearance of this symptom often beclouds any attempt to date the onset of the disease; however, careful study in a large group of patients has indicated that

* From the Section of Ophthalmology and the Section of Neurology, Mayo Clinic and Mayo Foundation. The Mayo Foundation, Rochester, Minnesota, is a part of the Graduate School of the University of Minnesota.

the disease usually begins in the second or third decade. The degree of abnormal sleepiness varies widely in different patients, ranging from rather persistent drowsiness with only infrequent episodes of sleep to moderate sleepiness which may cause the patient to fall asleep while driving, reading, watching television or viewing movies. In severe forms the patient may fall asleep during conversation, while eating or in unusual situations, such as when taking a shower or during sexual intercourse. Brief naps may alleviate the abnormal sleepiness but shortly after arousal, the narcoleptic person again drifts into a state of drowsiness from which he may sink into repeated episodes of sleep. We would emphasize, therefore, that the narcoleptic person spends much of his time suspended in a state of limbo, neither asleep nor fully alert. In contrast to the impression held in earlier years, there is no precipitous transition from full alertness to sleep; thus, narcoleptic sleep is in no way related to the abrupt transitions of consciousness seen in epilepsy.

Cataplexy, the second most frequent member-symptom of the tetrad, occurs in two thirds of patients and consists of muscular weakness induced by emotion. Cataplectic attacks are most commonly precipitated by laughter, anger, or surprise. The degree of muscular weakness ranges from a subjective sense of weakness to complete paralysis in which the patient collapses to the ground. Consciousness remains unchanged even in the face of total paralysis. The attack is short, rarely lasting more than a minute.

Sleep paralysis, which is analogous to cataplexy, occurs in a minority of patients. While patients are dozing or awakening, they may suffer transient inability to move. This paralysis is brief, and in most instances can be relieved by touching or speaking to the patient.

The last element of the tetrad is hypnagogic hallucinations which often accompany sleep paralysis. Hypnagogic hallucinations consist of visual or auditory sensations occurring in the drifting phase between sleep and wakefulness. The content of these hallucinations usually is benign. These experiences are analogous to the dreams that occur in many normal persons just prior to sleep.

Bearing in mind these clinical criteria for the diagnosis of the narcoleptic syndrome, let us turn to a consideration of the ocular complaints in these patients. The visual symptoms are of two major categories: first, inability to read for even short periods, and second, diplopia. In many patients complaints referable to reading lurk in varied guises; careful interrogation will clarify the precise nature of these complaints. An initial statement of the patient may be that his glasses need changing, that he has "weak eyes," that he suffers from "eyestrain," or that his eyes "tire easily." In many patients the fact that actual sleep follows upon any attempt to read may not emerge except upon close questioning. Some patients may report that after reading one or two pages they must "rest their eyes" or that watching television programs "tires" their eyes and that they must close them. Too ready acceptance of these statements from a narcoleptic patient may obscure the fact that such actions invariably are associated with sleepiness. A related complaint is the inability to stay awake while driving, an almost universal problem with narcoleptic persons. Again, in many instances, patients relate the difficulty in remaining alert while driving to presumed ocular fatigue associated with driving. Thus, the patient may come to the ophthalmologist seeking refraction in the hope that this will alleviate his difficulties.

Previously, few authors have commented upon intermittent diplopia as a symptom of narcolepsy. In 1925, Hilpert[3] reported the first example. Daniels[4] mentioned five patients who experienced diplopia immediately before falling asleep. In a review of the literature Levin[5] found only scattered references to diplopia and gave no quantitative data concerning the incidence of this phenomenon. From our interviews with a rather large

number of patients with narcolepsy, we have been impressed by the fact that these patients frequently experience intermittent diplopia when they are drowsy. For this reason we have undertaken an intensive ophthalmologic investigation of 25 consecutive patients with narcolepsy.

Materials and Methods

The series consisted of 11 males and 14 females 15 to 55 years of age. All patients included in this series were examined by the neurologists (Yoss and Daly) and referred for ophthalmologic study irrespective of the presence or absence of visual complaints. In this series the disease had made its appearance by the time the patients were aged 30 years or younger. By the criteria for selection 100 percent of the patients suffered from abnormal sleepiness. Sixteen patients (64 percent) reported attacks of cataplexy. Fifteen (60 percent) had experienced hypnagogic hallucinations and 13 (52 percent) had experienced episodes of sleep paralysis. The ratio according to sex observed in this group differs from that observed in our larger series.[1] No obvious reason exists for this disparity; presumably it represents nothing more than random variation due to the smallness of the sample.

The phoria and prism vergences of the 25 patients were measured at a visual distance of 15 feet and 15 inches. The heterophoria was measured by the prism-cover test and by the Maddox rod. Only the findings at the near visual distance are reported. All measurements were made by the same examiner. In no instance was there more than two diopters' difference between the Maddox-rod and the prism-cover measurements. In reporting the data we shall use the mean phoria measurements. Prism vergences were obtained by the use of the Risley prism at the same near-test distance.

Results

Of the 25 patients 10 had complained of intermittent diplopia. Nine patients had noted only blurring of vision while reading. Five patients had noted neither diplopia nor blurring of vision. One patient (Case 1 in Table 1) had noted diplopia only during attacks of cataplexy.

Of the 10 patients who complained of intermittent diplopia, nine had exophoria at near of eight diopters or greater, while only one patient (Case 20) with exophoria of less than eight diopters had experienced diplopia. This latter patient, although having merely an exophoria at near of two diopters, noticed doubling of vision immediately before sleep only if she was fixating upon a near object. For these 10 patients the maximal exophoria was 20 diopters and the median value for the group was 10 diopters.

In the second group of nine patients, who had noted blurring of vision but no frank diplopia, the exophorias ranged from two to 12 diopters at near. The median value was seven diopters of exophoria.

Five patients had experienced neither blurring of vision nor diplopia. Of these five, three patients had exophorias at near of five diopters, three diopters and two diopters, respectively. Two patients had esophoria at near of 1.5 diopters. The two patients with esophoria at near had minimal difficulty with drowsiness while reading. The median value for the phorias of these five patients was exophoria at near of two diopters. One patient with exophoria at near of three diopters had noted diplopia only during attacks of cataplexy.

In general, diplopia on reading apparently was related to marked exophoria, while blurring of vision was associated with only moderate exophoria. Interestingly, in the second group (blurring of vision) the patient (Case 16) with the highest exophoria, 12 diopters, had virtually ceased to read because of the severity of her narcolepsy; this may account for the minor character of her ocular symptoms.

Viewed from the reverse point of view, we may predict that any narcoleptic person who has exophoria of eight diopters or more will

TABLE 1

CHIEF OPHTHALMOLOGIC MANIFESTATIONS: 25 PATIENTS WITH NARCOLEPSY

Case	Age	Sex	Symptoms	Diplopia	Blurring	Before Treatment		After Treatment	
						Phoria	Vergence	Phoria	Vergence
1	16	F	N C SP HH	+*	+	3 X	24 I to 6 O		
2	45	M	N C	−	−	3 X	20 I to 24 O		
3	51	F	N C HH	+	+	14 X	22 I to 28 O	7 X	22 I to 30 O
4	41	F	N C SP HH	+	+	12 X	22 I to 16 O	7 X	22 I to 16 O
5	35	F	N SP HH	−	+	2 X	12 I to 22 O		
6	40	M	N C SP HH	−	+	2 X	17 I to 16 O		
7	47	M	N C HH	−	+	7 X	15 I to 28 O		
8	26	M	N C	−	+	4 X	16 I to 24 O		
9	42	M	N C	−	−	1.5 S	8 I to 30 O		
10	28	F	N C SP HH	−	−	2 X	18 I to 22 O		
11	42	M	N	+	+	8 X	15 I to 22 O	7 X	12 I to 24 O
12	55	F	N	+	+	20 X (T)†			
13	47	M	N HH	−	+	4 X	18 I to 30 O		
14	39	F	N C SP HH	+	+	9 X	20 I to 18 O		
15	35	F	N C SP HH	+	+	16 X	28 I to 8 O	16 X	26 I to 10 O
16	19	F	N C SP HH	−	+	12 X	10 I to 13 O	2 X	10 I to 30 O
17	52	F	N SP HH	+	+	13 X	19 I to 4 O	11 X	22 I to 4 O
18	40	F	N SP	−	−	1.5 S	30 I to 10 O		
19	33	M	N C SP HH	+	+	9 X	14 I to 24 O		
20	40	M	N	+	+	2 X	14 I to 28 O		
21	52	F	N C SP HH	+	+	8 X	15 I to 27 O	8 X	21 I to 30 O
22	15	F	N	−	−	5 X	12 I to 26 O		
23	63	M	N	−	+	8 X	28 I to 24 O		
24	42	M	N C SP HH	−	+	10 X	24 I to 8 O	Same	Same
25	48	F	N C	−	+	9 X	15 I to 14 O	3 X	18 I to 30 O

Explanation of symbols

N = Narcolepsy SP = Sleep paralysis X = Exophoria I = Base-in prism
C = Cataplexy HH = Hypnagogic hallucinations S = Esophoria O = Base-out prism
* Diplopia only with cataplectic attacks † Intermittent exotropia

suffer visual difficulty while reading. Conversely, a narcoleptic person with minimal exophoria or esophoria will read with few or no visual symptoms, although, it must be emphasized, the patient may still fall asleep frequently while reading.

In nine patients the tests were repeated after the patient had received an analeptic agent, methylphenidate (Ritalin). In two instances (Cases 15 and 24) the patient's symptoms were incompletely relieved; for this reason, we shall not include them in this portion of the study. Seven of these patients reported "good" to "excellent" relief of their abnormal sleepiness as well as striking improvement in their ability to read. In Cases 16 and 25 a marked increase in prism convergence and a decrease in the exophoria were noted. In Cases 3 and 4 a substantial reduction in the exophoria was noted. Three patients (Cases 11, 17 and 21) showed no significant change in their measurements.

COMMENT

Narcoleptic patients may present themselves to the ophthalmologist with vague and nonspecific ocular complaints such as "eyestrain," "weak eyes," difficulty in reading, or "tiring" of the eyes when watching motion pictures or television. Often the patient is convinced that refraction will resolve his difficulties. Failure to recognize that these complaints are manifestations of sleepiness will lead to misinterpretation of their significance. When it is appreciated that these activities invariably are associated with drowsiness, the physician's attention will then be directed to the basic disorder: abnormal and excessive sleepiness. Since these complaints may constitute the presenting symptoms of the patient, the ophthalmologist should be aware of them as clues to the correct diagnosis of narcolepsy.

In many instances, although the problem of excessive sleepiness remains in the back-

ground, the patient may formulate his symptoms more specifically and speak of blurring of vision or diplopia. In some patients a diagnosis of multiple sclerosis has been suggested by these complaints. In other instances the report of episodic diplopia in association with drooping of the eyelids has raised a suspicion of myasthenia gravis. In all such situations errors in diagnosis have resulted from preoccupation with isolated symptoms instead of consideration of the complete clinical picture. Careful questioning of the narcoleptic patient concerning his blurring of vision or diplopia would disclose that it was brief in duration, often had occurred while performing close work which required convergence of his eyes and invariably was associated with drowsiness or brief episodes of sleep.

Recognition by the ophthalmologist of the basic disorder of excessive sleepiness which underlies the patient's complaints is of great practical value to the patient, since effective analeptic drugs are available to treat narcolepsy. In our experience[2] methylphenidate (Ritalin) administered in doses of 20 mg. three or four times daily will control satisfactorily the excessive sleepiness of most patients. When the patient is maintained in a state of normal alertness throughout the day, his visual difficulties disappear.

From a theoretic point of view, the present study gains additional interest since it elucidates the mechanism of production of visual symptoms in these patients. The patient's difficulty in reading apparently depends upon the severity of the narcolepsy and the degree of exophoria. The mechanical act of reading is a boring and monotonous process, since it involves the repetitive movement of the eyes with a minimum of extraneous stimuli.

Narcoleptic persons are well aware that performance of monotonous and repetitious tasks, particularly in the absence of any stimuli from the environment, will consistently cause them to fall asleep. The more severe the narcolepsy, the more readily will this happen, even if the narcoleptic person earnestly desires and indeed struggles to stay awake. For this reason, patients with severe narcolepsy will fall asleep so frequently while attempting to read that many finally cease to read. Such patients often confuse the unwary examiner with a denial of any difficulty in reading, when they actually mean that they no longer read.

Patients who are less seriously troubled with narcolepsy may be reluctant to admit that they can read little more than the headlines of the newspaper before dozing off, or that a single chapter of a book defeats them so that reading an interesting novel may require several months of effort.

This difficulty is entirely independent of any visual symptoms, such as blurring of vision or diplopia which can occur when the patient becomes drowsy. If, in addition to his narcolepsy, the patient has exophoria, our findings suggest that when he is drowsy he will note diplopia, if the degree of exophoria is marked, or blurring of vision, if the exophoria is mild. Thus, difficulty in maintaining a state of alertness reflects the severity of the narcolepsy, while blurring of vision or diplopia when in a state of impaired alertness, such as drowsiness, depends upon the concomitant presence of exophoria.

We would emphasize that the diplopia and blurring of vision are not manifestations of any structural lesion in the visual apparatus, but rather are consequences of the abnormal physiologic state of sustained drowsiness. Similar blurring of vision or even diplopia can develop in normal persons during states of severe sleepiness which are analogous to the customary state of the narcoleptic person.

These hypotheses are reinforced by observations on the effect of treatment in the narcoleptic person. Although the exophoria seemed to decrease in four of the patients who took Ritalin, we believe this decrease to be more apparent than real, since the measurements were not made in comparable physiologic states of alertness. The situation here is analogous to the results of determinations

of basal metabolic rates in narcoleptic patients.

In many narcoleptic patients basal metabolic rates will be obtained which seem abnormally low; however, objective measurements of thyroid function do not substantiate the presence of hypothyroidism. If it be realized that the narcoleptic patient readily becomes somnolent and drowses off while following the instructions to lie quietly with his eyes closed during the determination of his basal metabolic rate, then it is clear that his state is no longer "basal." Such lowered consumption of oxygen thus is not abnormal but simply indicative of the normal decline in activity with sleep.

The analogous loss of the ability to maintain fusion in a normal person who is markedly drowsy has been long known but the present study is unique since it furnishes objective measurements of this phenomenon. Any efforts to obtain such measurements in a normal person would necessarily fail, since the mere attempt at measurement would rouse him from his drowsy state to an alert state. The narcoleptic person, because of his abnormal degree of drowsiness, can remain suspended in the twilight state between full wakefulness and sleep long enough to permit such observations.

The Mayo Clinic.

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RO 1-7683/15: A NEW AND EFFECTIVE MYDRIATIC

Héctor M. Nano, M.D., O. Gavarini, M.D., and Humberto A. Pérez, M.D.
Buenos Aires, Argentina

Examination of the eyeground has become a routine ophthalmic procedure and a valuable diagnostic aid. The use of mydriatics, among them homatropine hydrobromide (one-percent solution) is most widespread.

Practically all mydriatics dilate the pupil sufficiently for funduscopy, yet some difficulties arise that lead at times to restriction in the use of these drugs. Two disadvantages are that they take considerable time to produce mydriasis, especially in older persons, and it takes time for the dilated pupil and for accommodation to return to normal. Any new preparation that will eliminate these disadvantages is welcomed. At present, the visual disturbances brought about by the so-called quick-acting mydriatics require 24 hours to clear. Many patients find this exceedingly annoying, with the result that they dislike using mydriatics or any collyrium, which could constitute a therapeutic drawback of some importance.

This is why, although skeptical, we made a thorough study of a new mydriatic collyrium, manufactured by F. Hoffmann-La Roche S.A., which was said to have none of the disadvantages of other mydriatics in current use.

Procedure and Results

We experimented with the isotonic aqueous solutioins of Ro 1-7683 (five percent), no other collyrium having been previously instilled (except in special cases to be mentioned). In all instances care was taken to reproduce the conditions of every-day practice. Patients with conjunctival or anterior segment complaints—whether acute, sub-

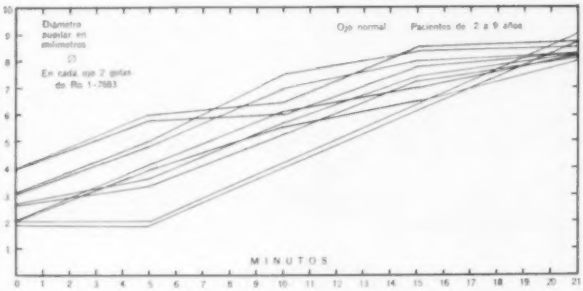


Fig. 1* (Nano, et al.). Normal eyes of patients aged two to nine years.

* Pupil diameter in millimeters in Figures 1 through 18. Figures 1 through 7, two drops of Ro 1-7683.

acute or chronic—were ruled out, as were patients with continual or transient lacrimation.

With such criteria, the following observations were made:

1. *Influence of age.* The mydriatic effects of Ro 1-7683 were measured in several age groups of 10 subjects each, ranging from the first to the seventh decade. Graphs 1 to 7 show it to be active at all ages, though slightly less rapid after the age of 60 years. Graph 8 shows the average curve, for all these cases.

2. *Speed of action in normal eyes.* Graphs 1 to 8 show that, as a rule, mydriasis began five minutes after two drops of Ro 1-7683 were instilled into the conjunctival sac, the pupils reaching a diameter of from five to six mm. about five or 10 minutes later.

3. *Comparison with homatropine hydrobromide (one-percent solution).* The mydriatic effects of both drugs were tested on different subjects, then in turn on one and the same subject. As shown in Graph 9, faster and greater dilation was observed following the instillation of Ro 1-7683. Moreover, this drug is so well tolerated that it can be employed in almost all instances where mydriasis is desired.

4. *Comparison with Dilatol.* The mydriatic effects of both these drugs were compared on different subjects first, and then in turn on one and the same subject. Graph 10 shows the indisputable superiority of Ro 1-7683 over C.L. α-hydroxy-β-methylamine-3 hydroxy-ethyl-benezene (Dilatol), a mydriatic widely used in some countries.

5. *Effects of Ro 1-7683 after instillation of one drop or of two drops at 10-minute intervals.* Groups of five patients each were tested. In all instances, a greater degree of mydriasis was observed at a faster rate after instilling two drops of Ro 1-7683 into the conjunctival sac (graph 11).

6. *Return of the dilated pupil to its original size.* Graph 12 shows this was accomplished in four patients from eight to nine hours after two drops of Ro 1-7683 were instilled into the conjunctival sac.

7. *Return of the pupil to original size: Ro*

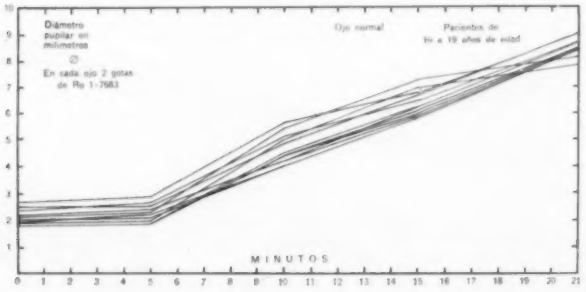


Fig. 2 (Nano, et al.). Normal eyes of patients aged 10 to 19 years.

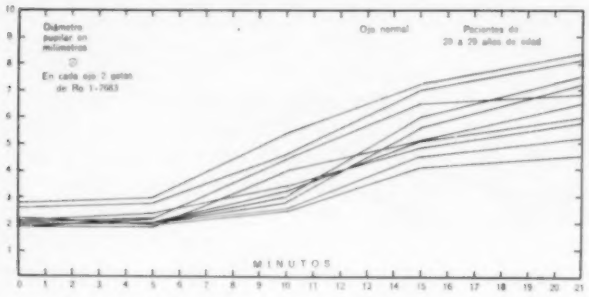


Fig. 3 (Nano, et al.). Normal eyes of patients aged 20 to 29 years.

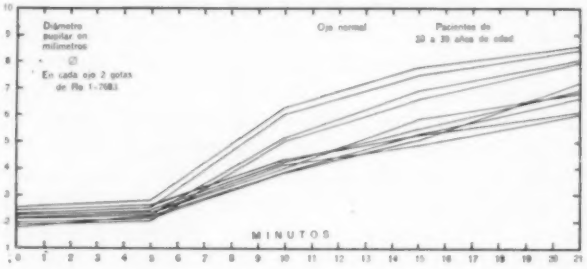


Fig. 4 (Nano, et al.). Normal eyes of patients aged 30 to 39 years.

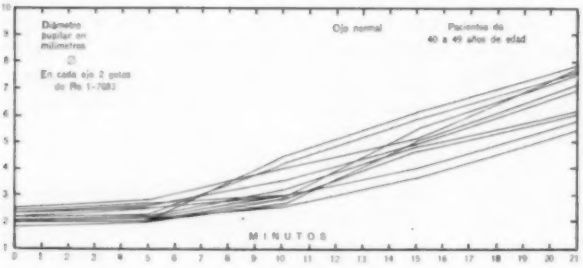


Fig. 5 (Nano, et al.). Normal eyes of patients aged 40 to 49 years.

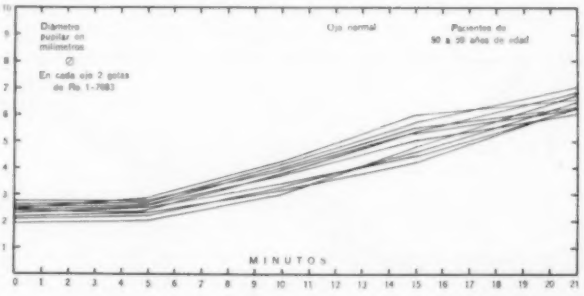


Fig. 6 (Nano, et al.). Normal eyes of patients aged 50 to 59 years.

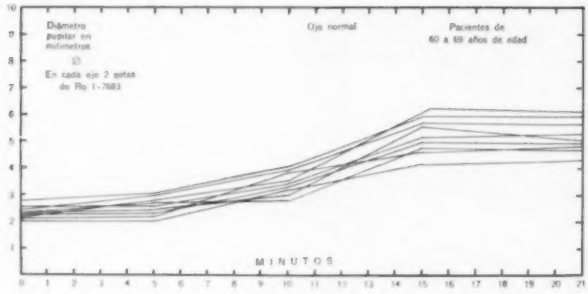


Fig. 7 (Nano, et al.). Normal eyes of patients aged 60 to 69 years.

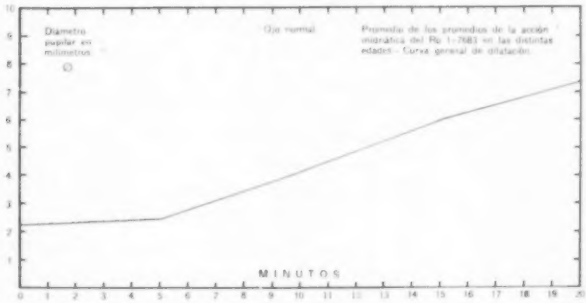


Fig. 8 (Nano, et al.). Effect of Ro 1-7683 in all normal eyes tested.

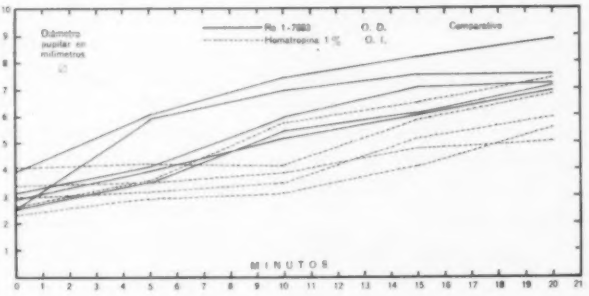


Fig. 9 (Nano, et al.). Comparison of Ro 1-7683 and one-percent homatropine.

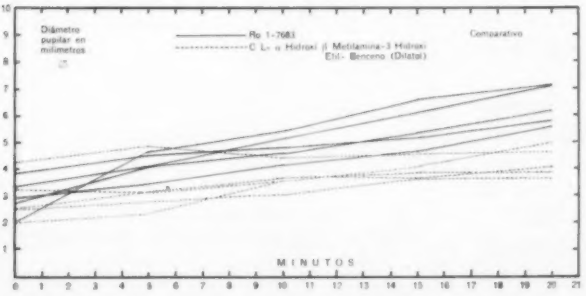


Fig. 10 (Nano, et al.). Comparison of Ro 1-7683 and Dilatol.

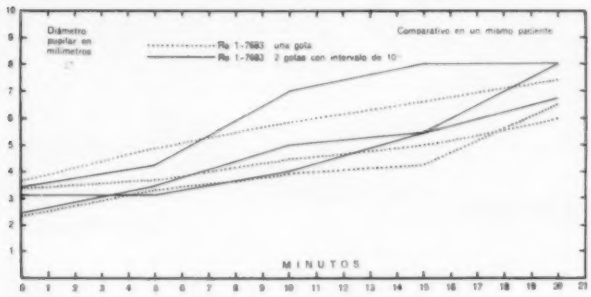

Diámetro pupilar en milímetros
Comparativo en un mismo paciente
Ro 1-7683 una gota
Ro 1-7683 2 gotas con intervalo de 10'
MINUTOS

Fig. 11 (Nano, et al.). Comparison of one drop of Ro 1-7683 and two drops of Ro 1-7683.

1-7683 and homatropine compared. Numerous curves were obtained following instillation of two drops of Ro 1-7683 into one eye, and of two drops of a one-percent solution of homatropine into the other eye of several patients. Graph 13 shows curves for eight patients in whom typical results were observed. One dotted and one continuous line represents each patient. It is apparent that, after the pupil dilated by Ro 1-7683 has returned to its original diameter, the homatropinized pupil is still widely dilated. Disturbance of accommodation—so vexing to most patients—paralleled to some degree the mydriasis observed.

8. *Mydriasis in dark eyes and in light-colored eyes.* Graph 14 points to no sizable difference in the reaction of either kind of irises. Nevertheless, it was our impression that the effects of Ro 1-7683 are greater on light blue eyes.

9. *Comparison of Ro 1-7683 and homatropine as used for diagnosis on aphakic eyes.* We experimented on one patient with postoperative bilateral aphakia. As shown on Graph 15, quicker and better mydriasis was obtained by means of Ro 1-7683 than with homatropine.

10. *Mydriasis with Ro 1-7863 in patients with a pathologic fundus.* Ro 1-7683 was instilled bilaterally, then unilaterally for comparison with a standard mydriatic. Graph 16 shows that the curves obtained in patients with pathologic fundi do not differ strikingly from those obtained in patients with normal fundi. Graph 17 shows the effects of Ro 1-7683 compared to those of homatropine (one-percent solution) as recorded on patients aged 55 to 60 years suffering from diabetic retinopathy in its third stage. Although differences are not marked, the advantage is clearly on the side of Ro 1-7683.

11. *Time required to obtain effective mydriasis for routine funduscopy.* Mydriasis is called effective when inspection of the fundus of the eye becomes practicable by means of a standard ophthalmoscope and the static measure of the pupil can be obtained with the Goldmann slitlamp. As the pupillary diameter, and so forth had previously been measured in all patients with the Goldmann slitlamp—which emits a very strong beam of light—we deemed it interesting to measure the time during which we were able to examine the fundus through an ophthalmoscope

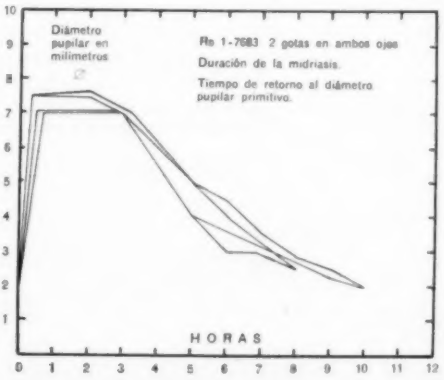

Diámetro pupilar en milímetros
Ro 1-7683 2 gotas en ambos ojos
Duración de la midriasis.
Tiempo de retorno al diámetro pupilar primitivo.
HORAS

Fig. 12 (Nano, et al.). Time of return of pupil to original diameter after two drops of Ro 1-7683.

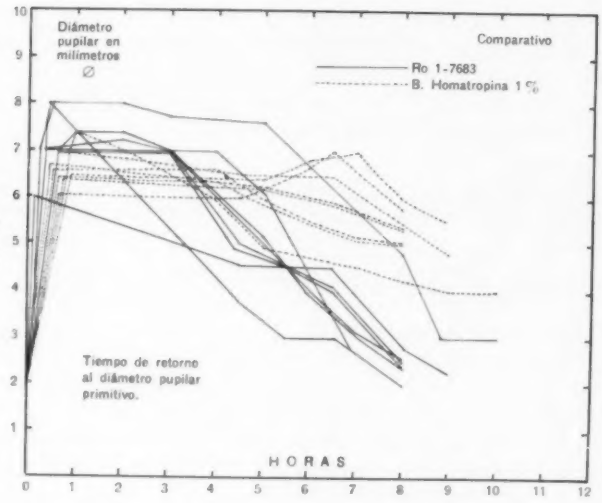


Fig. 13 (Nano, et al.). Comparison of Ro 1-7683 and homatropine in return of pupil diameter to original size.

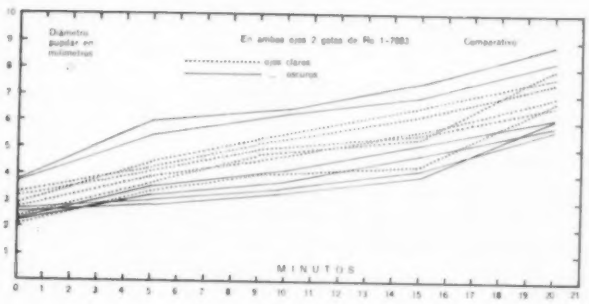


Fig. 14 (Nano, et al.). Mydriasis and light and dark eyes.

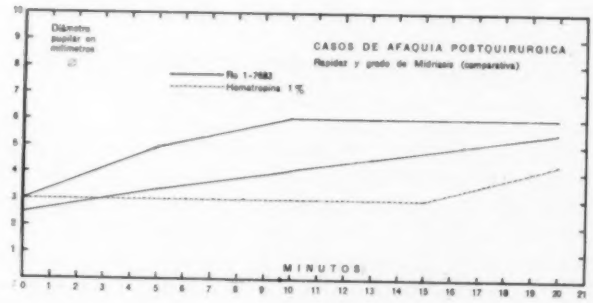


Fig. 15 (Nano, et al.). Comparative chart, showing rapidity and grade of mydriasis in a case of postsurgical aphakia.

after the instillation of two drops of Ro 1-7683 and before the contraction of the sphincter iridis, caused by the direct light reflex, should prevent us from continuing. The diameter of the pupil, as measured with the Goldmann lamp and with the Welch-Allyn ophthalmoscope, is shown on Graph 18.

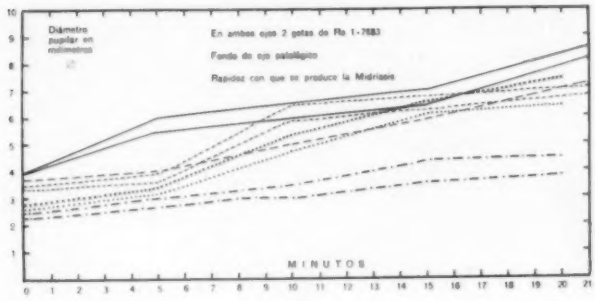
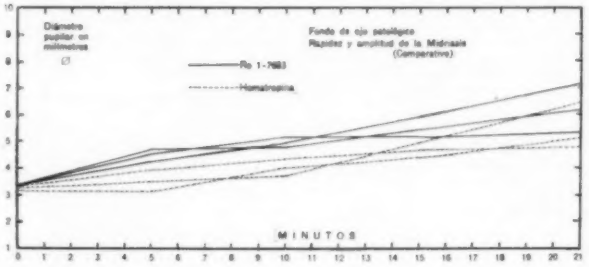

Diámetro pupilar en milímetros
En ambos ojos 2 gotas de Ro 1-7683
Fondo de ojo patológico
Rapidez con que se produce la Midriasis
MINUTOS

Fig. 16 (Nano, et al.). Study of cases with pathologic alterations of the fundus. - - - -, patient aged 57 years, obstruction of central retinal vein; ————, patient aged 20 years, bilateral papillary edema; - - - -, patient aged 40 years, renal retinopathy; . . . . . , patient aged 35 years, posttraumatic papillary atrophy; - . - . - , patient aged 55 years, third-degree diabetic retinopathy; . - . - . - . - , patient aged 62 years, fourth-degree diabetic retinopathy; x x x x, patient aged 27 years, malignant myopia.

Fig. 17 (Nano, et al.). Comparison of Ro 1-7683 and homatropine in rapidity and effectiveness of mydriasis in patients with pathologic fundus alterations.



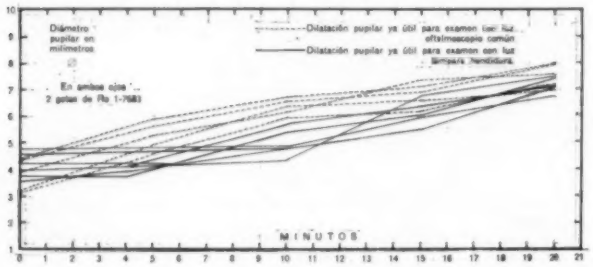

Diámetro pupilar en milímetros
En ambos ojos
2 gotas de Ro 1-7683
Dilatación pupilar ya útil para examen con luz oftalmoscopio común
Dilatación pupilar ya útil para examen con luz lámpara hendidura
MINUTOS

Fig. 18 (Nano, et al.). Effectiveness of mydriasis for routine funduscopy.

12. *Effects of Ro 1-7863 following instillation of standard collyria.* Ro 1-7683 was instilled into the conjunctival sacs of patients with normal fundi, following the instillation of Hyalase (4,000 Bender units dissolved in 10 cc. normal saline solution), or cocaine or pantocaine in one-percent solution, or antibiotic solutions in some instances. Since no considerable differences were observed in the time and the degree of pupil dilatation, no graphs have been included for consideration.

13. *Comparing the cycloplegic effects of Ro 1-7683 and of atropine sulfate on children's eyes.* By means of comparative static retinoscopy we investigated in children's eyes the paralysis of accommodation resulting from the instillation of a solution of one-percent atropine into one eye and of Ro 1-7683 into the other eye. The paresis of accommodation due to Ro 1-7683 precedes mydriasis and becomes very marked 10 minutes after instilling two drops of this collyrium;

for this reason it is undoubtedly useful in children, whether suffering from strabismus or not, on whom static refraction is to be performed. By instilling two drops of Ro 1-7683 every 15 minutes three times, accommodation was paralyzed to a degree comparable to that obtained by means of a solution of atropine sulfate instilled for several days. We performed the following representative treatment repeatedly.

A solution of one-percent atropine and Ro 1-7683 were instilled into eyes known to have equal refraction. A like degree of cycloplegia was obtained in both eyes. To ascertain its efficacy, a solution of 0.5 percent atropine was instilled every 12 hours for two days into the eye in which Ro 1-7683 had been used: the static retinoscopic readings obtained under similar conditions remained unchanged. (K. Staenglen, working at the Ophthalmologic Clinic of Hamburg University, Eppendorf, directed by Prof. H. Sautter, has reached similar conclusions).

14. *Effects of Ro 1-7683 on intraocular pressure in normal eyes.* A raise in intraocular pressure was observed in three patients with normal eyes following the instillation of two drops of Ro 1-7683 into each eye (graph 19). This mydriatic drug exerts no influence whatever on intraocular pressure, as the slight variations observed were doubtless due to the normal diurnal oscillation. Therefore, this collyrium should not be employed as a mydriatic for provocative tests.

15. *Effects of Ro 1-7683 on eyes suspected of having glaucoma, as compared with Priscol (Leinfender's test).* The efficacy of Ro 1-7683 compared to Priscol, when used as provocative agents to determine definitely whether or not glaucoma was present, was investigated in three patients in whom this disease was suspected. Two drops of Ro 1-7683 were instilled into the right conjunctival sac every five minutes for three times. Leinfender's test was performed on the left eye. In one of the instances, in which a positive Priscol test was observed, the right eye subjected to Ro 1-7683 underwent a decrease in tension (possibly coincident with the diurnal oscillation). Although undoubtedly further investigation on a large number of patients is in order, the fact deserves mention that Ro 1-7683 has not increased intraocular pressure either in normal eyes or in eyes suspected of glaucoma or suffering from preglaucoma or confirmed glaucoma. This added advantage justified its preference to other mydriatics.

16. *Hypertensive effects of Ro 1-7683 on glaucomatous eyes.* The increase in intraocular pressure following the instillation of two drops of Ro 1-7683 every five minutes for three times into each conjunctival sac was observed in patients suffering from chronic simple glaucoma who were to be operated on from two to three hours later. Intraocular pressure ranged from 30 to 55 mm. Hg (Schiøtz). Miosis was present in some instances owing to antiglaucomatous drugs; moderate pupil dilatation was observed from 10 to 20 minutes after Ro 1-7683 was instilled for the first time; no elevation in intraocular pressure was observed. Graph 20 shows two of the curves obtained.

17. *Ro 1-7683 as an iridodilator in the operation for cataract.* Ro 1-7683 was found an effective iridodilator for cataract operations.

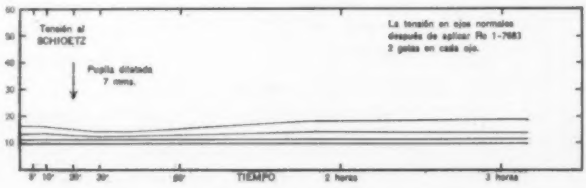

Tensión al SCHIOETZ
Pupila dilatada 7 mms.
La tensión en ojos normales después de aplicar Ro 1-7683 2 gotas en cada ojo.
TIEMPO
2 horas
3 horas

Fig. 19 (Nano, et al.). Tension study of normal eyes after two drops of Ro 1-7683.

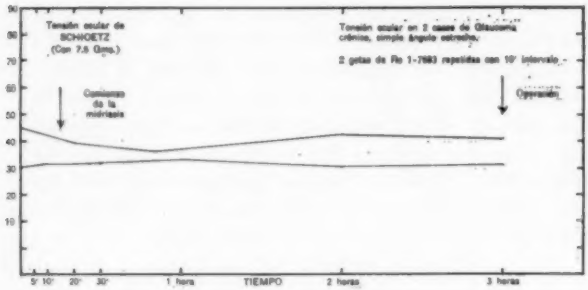


Fig. 20 (Nano, et al.). Tension studies in two cases of chronic simple glaucoma.

The degree of mydriasis obtained with Ro 1-7683 is excellent, does not diminish after the anterior chamber is opened, and its effects are sufficiently short acting to insure a quick return to the original pupillary diameter.

18. *Ro 1-7683 used as a nonhypertensive mydriatic in inflammatory or postinflammatory glaucoma.* Two drops of Ro 1-7683 were instilled three times in one day into the conjunctival sacs of three patients suffering from secondary inflammatory and postinflammatory glaucoma as a therapeutic measure; intraocular pressure was checked every 12 hours for three days. Ro 1-7683 combined with cortisone collyrium was found effective in the treatment of inflammatory glaucoma, as it maintained a moderate degree of mydriasis with no concomitant increase in intraocular pressure. Further research on a larger number of patients is necessary in order to be able to determine the actual effects of Ro 1-7683 in this respect.

19. *How Ro 1-7683 was tolerated.* We observed each patient for any ill-effects of this drug. It was found to be perfectly tolerated in all age groups and in patients with either normal or pathologic fundi. It causes no burning sensation. No after-effects were recorded.

Summary

We have experimented with Ro 1-7683/15, a mydriatic drug manufactured by F. Hoffmann-La Roche S.A., in 0.5 percent solution. It has been found effective both for diagnostic purposes and as a cycloplegic in the performance of refraction.

The advantages of Ro 1-7683 over current mydriatics are:

a. It is quick acting and effective in all age groups (graphs 1 to 8). A good view of the fundus of the eye is obtained 10 to 15 minutes after instillation.

b. Its mydriatic effects are stronger and faster than those of homatropine hydrobromide (graph 9) and of less common mydriatics (graph 10).

c. The return of the pupil to its original diameter takes place within eight or nine hours after instillation, whereas standard mydriatics take about 24 hours (graph 12).

d. In light-colored eyes, maximal mydriasis is sometimes observed, the iris becoming a thin circular line.

e. In aphakic patients, Ro 1-7683 produces greater mydriasis than any other mydriatic we have used (graph 17).

f. In eyes with pathologic fundi, Ro 1-7683 produces a degree of pupil dilatation similar to that obtained in normal eyes. Effective mydriasis (that is, permitting inspection with a standard ophthalmoscope) is achieved from seven to 10 minutes following instillation (graph 18).

g. The effects of Ro 1-7683 remain unaltered if standard mydriatics have previously been instilled into the conjunctival sac.

h. In a few minutes Ro 1-7683 paralyzes accommodation to an extent which a solution of 0.5-percent atropine can produce only when instilled for several days in succession.

i. Ro 1-7683 does not elevate intraocular pressure in normal eyes.

j. Ro 1-7683 does not elevate intraocular pressure in preglaucoma; neither has an increase in tension been observed in the few cases of chronic simple glaucoma examined. There is little or no risk of a dangerous elevation in tension.

k. Ro 1-7683 is useful in the operation for cataract.

l. In inflammatory glaucoma, when avoidance of synechias is desired, Ro 1-7683 is an extremely effective agent.

Conclusions

The fundamental indication of Ro 1-7683 arises when a mydriatic drug is required for diagnostic purposes. Its use in cases of preglaucoma or probable glaucoma is indispensable. The quickness of its effects makes it very useful when rapid mydriasis is desired. Owing to its fast action on accommodation, it will in all probability become widely used for performing routing retinoscopy on children. Though no elevation in intraocular pressure has been observed in patients suffering from glaucoma and probable glaucoma, it would seen wise to protect patients with Diamox administered simultaneously. Ro 1-7683 is the collyrium of choice when ophthalmoscopy must be performed on a glaucomatous eye. (In many clinics it is advised to dilate the pupils of glaucomatous patients once a year in order to examine the eyes thoroughly.) We are convinced that its many advantages will make the use of this new mydriatic widespread.

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THE CLINICAL APPLICATION OF THE GOLDMANN APPLANATION TONOMETER

Theo A. F. Schmidt, M.D.
Bern, Switzerland

Measurement of pressure in an enclosed space is subject to an important source of error. Namely a change of volume is generally necessary before a reading from the pressure-indicating instrument can be obtained. This change of volume alters the original pressure. To measure the original pressure as accurately as possible, the change of volume must either be compensated or limited to insignificant proportions. Where neither of these methods can be used, the change of volume and the law determining the change of pressure with volume must be accurately known. An ideal instrument for measuring the intraocular pressure would be a compensated membrane manometer or a strain gauge. Equipment of this type cannot of course be used on the living human eye and we are therefore confined to the use of so-called tonometers which may take the form of indentation or applanation tonometers, impression or applanation changes the intraocular pressure, while the increased pressure, P_t, partially created by the instrument is measured by it.

In the application of impression tonometry, that is to say, taking measurements with the Schiøtz, McLean or Gradle tonometers, the reading of the instrument is significantly affected by the scleral rigidity as well as by the intraocular pressure. Unless the tonometers used are absolutely identical, the deflections obtained from one and the same eye are bound to vary. This is the reason for the extreme care necessary in standardizing Schiøtz tonometers, although fresh sources of error resulting in deviations of the measured result are continually being discovered.

It must also be realized that the relationship between the instantaneous intraocular pressure P_t, and the depth of indentation

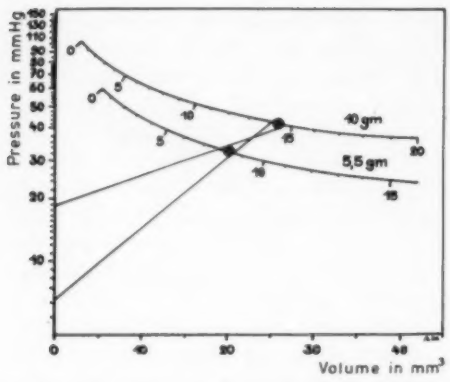

Fig. 1 (Schmidt). Influence of the measuring error on the estimation of scleral rigidity coefficient and P_o value.

for any given instrument is established on the basis of a purely empirical formula whose constants must be determined by careful, time-consuming tests. The difficulties involved are best illustrated by the fact that the established P_t values have had to be changed several times since 1948. The volumetric displacement created by a Schiøtz tonometer on being placed in contact with the eye is of the order of 6.0 — 30 mm.^{3}, covering a measuring range of between 10 and 30 mm. Hg, depending on reading and weight. Here again, it is extremely difficult to determine the precise value of the displaced volume. An expression was finally developed by Friedenwald which enables the initial pressure P_o to be calculated from two P_t values with different volumetric displacements (using two Schiøtz weights). The relationship between P_t and P_o depends on the rigidity characteristic of the individual eye. In actual practice it is very difficult to determine the P_o value and the rigidity of the bulbar wall, since each measurement is subject to a relatively great error (fig. 1). In most cases, the P_o value is simply taken from a single measurement interpreted by means of calibration scale, which is valid only for eyes with an average coefficient of ocular rigidity. This leads to serious measuring errors especially in myopic eyes, as we were able to demonstrate. The fact that the common volumetric displacement applies only to eyes with a normal corneal curvature, gives rise to yet another set of difficulties relating to eyes with microcornea and megalocornea.

In the application technique with the Goldmann tonometer (fig. 2), the effect of scleral rigidity is eliminated. The flattened area is very small with the Goldmann applanation tonometer and therefore the displaced volume is insignificant. For all practical purposes $P_t = P_o$. This is illustrated by the values in the table (table 1), which shows that, depending on the rigidity and the corneal radius, the true P_o values may differ greatly from the tabulated values when using the Schiøtz tonometer. One will realize that unless the ocular rigidity and the corneal curvature radius are known, the measured result is likely to be subject to considerable error. Cases in which the rigidity and corneal curvature radius are such that they result in very large errors, are comparatively rare but you can see from the right portion of the

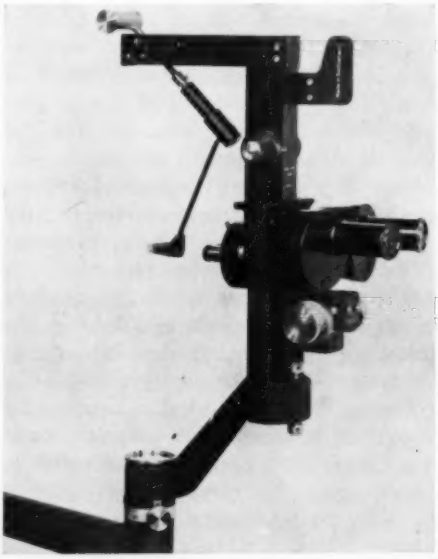

Fig. 2 (Schmidt). The Goldmann applanation tonometer.

TABLE 1

VALUES OBTAINED WITH SCHIØTZ AND GOLDMANN TONOMETERS

Corneal Radius	Schiøtz Tonometer weight 7.5 gm. reading 5.0 P_t = 42.6 mm.Hg			Applanation Tonometer reading on the measuring drum P_t = 26.5 mm.Hg		
	Rigidity			Rigidity		
	0.0050	0.0215	0.0350	0.0050	0.0215	0.0350
4.5	29.1	8.3	3.0	26.2	25.2	24.5
7.8	37.9	25.8*	18.8	26.3	25.8	25.3
15.5	40.8	35.2	31.2	26.3	26.1	25.9

* According to calibration table 1955 (Friedenwald).

table that such extreme conditions have a much smaller effect on the result when the applanation tonometer is used.

What is the reason for this? It is simply due to the very small increase of pressure during measurement, or in other words, to the very small difference between the P_o and P_t values. Why is the difference between the P_o and P_t values so small? Because of the small volumetric displacement during measurement. It is seen from the next nomogram (fig. 3) that the effect of changes in rigidity increases with an increasing change of volume. A second line, located near the zero line at 0.56 mm.³ indicates the volumetric displacement produced by the applanation tonometer. The small triangle at the point A shows the small influence of scleral rigidity

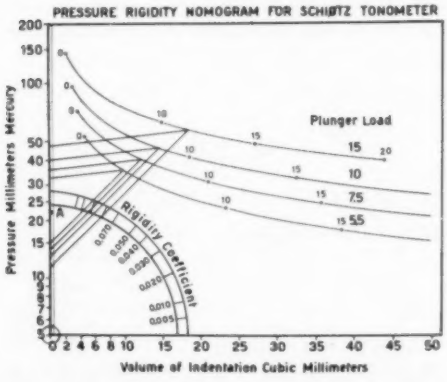

Fig. 3 (Schmidt). The range of P_o values, which may correspond to a single measurement with Schiøtz tonometer is larger with larger displaced volume.

on P_o as measured by the applanation tonometer. The precise volume displaced by the applanation tonometer also depends on the corneal curvature radius but varies only slightly as shown in the Table 2.

The difference between P_o and P_t values amounts to 2.7 percent in normal cases and to only 7.7 in the least favorable case of increased rigidity and small corneal curvature radius (table 3). This means that with a measured value of 20 mm. Hg, the intraocular pressure under these conditions amounts to 18.5 mm. Hg, with a P_t value of 25, the P_o value amounts to 23.1 mm. Hg. You can see that even in extreme cases, the P_t value obtained by applanation tonometry with the Goldmann tonometer can with every justification be assumed to be equal to the P_o value. The fact that the rigidity coefficient has no practical significance in applanation tonometry is shown quite clearly in the Figure 3. The dispersion area of the rigidity coefficients are represented as angles. The

TABLE 2

RELATIONSHIP BETWEEN CORNEAL CURVATURE AND DISPLACED VOLUME BY APPLANATION TONOMETRY WITH 3.06-MM. DIAMETER

Radius of Corneal Curvature in mm.	Volume in mm³.
4.5	0.995
5.5	0.804
6.5	0.675
7.5	0.582
8.5	0.512
9.5	0.457
10.5	0.412
15.5	0.281

TABLE 3

DIFFERENCE BETWEEN P_0 AND P_t VALUES PERCENT, DEPENDING ON CORNEAL CURVATURE AND SCLERAL RIGIDITY

Radius of Corneal Curvature in mm.	Scleral Rigidity		
	0.0050	0.0215	0.0350
4.5	1.14	4.81	7.7
5.5	0.92	3.97	6.27
6.5	0.86	3.28	5.29
7.5	0.67	2.80	4.58
8.5	0.59	2.50	4.04
9.5	0.53	2.24	3.62
10.5	0.47	2.02	3.27
15.5	0.32	1.78	2.24

nearer the measuring point approaches the zero line, the smaller will be the spread. With the applanation tonometer the measuring point is located in the immediate neighborhood of the zero line, as already mentioned.

The question arises, how important it is to know the scleral rigidity, or in other words, how often does the actual intraocular pressure vary significantly from the value measured with one plunger weight of the Schiøtz tonometer and given in the table for P_o based on the assumption of average scleral rigidity ($E = 0.0215$). We have measured the scleral rigidity of 384 glaucomatous eyes using the applanation tonometer and the Schiøtz tonometer with the 7.5 plunger load. These included operated and unoperated, old and young glaucoma patients, as they consulted our clinic. The mean value of scleral rigidity of these 384 eyes was 0.01908 with a standard deviation of $\sigma = \pm 0.005808$.

Table 4 shows that if the Schiøtz tonometer scale reading were 5.3 with the 7.5 gm. weight the $P_o = 25$ mm. Hg from the Friedenwald table, 1955, but only 31.5 percent of the patients would actually have an intraocular pressure between 23.5 and 26.5 mm. Hg. Table 4 shows also that in a large percentage of glaucoma patients serious errors would be made, if reliance is placed on the measurement with a single plunger weight and scleral rigidity is not considered. In our experience, particularly in cases after operation, scleral rigidity is lowered and the Schiøtz tonometer indicates a pressure lower than actually exists.

Large variations of the corneal curvature are less frequent than variations of scleral rigidity, so that in general considerable errors of the P_o value using one Schiøtz weight are less influenced by corneal curvature than by scleral rigidity. In 1928 Leibowicz made a study of the corneal curvature of 10,330 astigmatic eyes which were measured with the ophthalmometer of Javal-Schiøtz. We have used this material for our calculations. A scale reading of 5.3 of the Schiøtz tonometer with 7.5 gm. plunger load corresponds in the Friedenwald table of 1955 to an intraocular pressure of 25 mm. Hg assuming a mean value of scleral rigidity of 0.0215 and a mean value of corneal curvature of 7.8 mm. as already mentioned.

In 92.1 percent of the population the corneal curvature varies between 7.3 and 8.25 mm. This variation in corneal curvature would produce a variation in intraocular pressure between 26 and 24 mm. Hg at a scale reading of 5.3/7.5 gm. In 7.9 percent of the population the intraocular pressure would be more than 26 and less than 24 mm. Hg, in other words the error would be greater than $\pm$ 1.0 mm. Hg. In 1.1 percent the error is greater than $\pm$ 2.0 mm. Hg. These numbers are valid only for eyes with a mean value of scleral rigidity. If the scleral rigidity varies from this mean value, then greater or smaller total errors are to be expected. It is useful to know the corneal curv-

TABLE 4

VARIATIONS IN TONOMETER READINGS

Variation from the Table Value 25 mm.Hg = 5.3/7.5 gm. (mm.Hg)	%
$< \pm$ 1.5	31.5
$> \pm$ 1.5	68.5
$> \pm$ 3.0	43.0
$> \pm$ 4.5	26.0
$> \pm$ 6.0	14.0
$> +$ 7.5	8.0
$> +$ 9.0	4.0
$> +12.5$	1.0

ature in any case of microcornea or megalocornea, when the Schiøtz tonometer is used. I would like to point out that scleral rigidity and corneal curvature have negligible influence, when the applanation tonometer is used so that it is not necessary to measure them.

There are a number of other questions which I should like to discuss:

From what has been said so far, it will be clear that the Goldmann applanation tonometer is superior to the Schiøtz tonometer. However, is the applanation technique intrinsically superior to the impression technique? The applanation technique is not very new; the Maklakoff applanation tonometer is still used in Russia. If it is really superior to the impression technique, why have applanation tonometers not generally been accepted?

The basic expression for applanation tonometry is very simple; it is based on the relationship $\frac{W}{A} = P_t$ or weight divided by area equals pressure. However, as the area is expressed in terms of diameters, any error involved will be magnified by the square of its value.

Errors occur frequently because the lacrimal fluid surrounding the cornea is included in the measurement. These errors decrease with an increasing applanation effect, but relatively large flattened areas are accompanied by correspondingly large volumetric changes and the ocular rigidity errors are similar to those of the Schiøtz tonometer. Moreover, buckling of the cornea and its capillary liquid film must be included in the calculation, as demonstrated by Goldmann. All these features resulted in the old applanation tonometers being no better than the Schiøtz tonometers, and indeed being a great deal worse.

If these factors can be taken into account and the amount of flattening (although very small) can be accurately measured, the applanation tonometer will undoubtedly be superior to the old applanation and also to the indentation tonometer. This was in fact achieved in the Goldmann tonometer.

The instrument itself

The Committee on Standardization of Tonometers found after many years of investigation that the measured results obtained with the Schiøtz tonometer depended on about 20 different dimensions and characteristics of the instrument, quite apart from the physiologic conditions of the eye. In the design of a tonometer, a certain tolerance limit must be assumed for each dimension; the effect of these permissible deviations may well be cumulative in one direction, so that a Schiøtz tonometer, although conforming to specification, may yet have an overall error amounting to $\pm$ 3.0 scale divisions, as calculated by Albrecht and his collaborators.

Although this extreme case does not often occur, an instrument error amounting to $\pm$ 1.0 scale unit is by no means rare. What is the corresponding position of the applanation tonometer?

Apart from friction between moving parts, there are only two points through which the instrument itself may affect the measured result: Firstly, the little prism of plastic material (fig. 4) for measuring the flattened corneal area and secondly, the balance which measures the force required to produce the specified amount of flattening or applanation. The actual prism incorporates two prisms which divide the image in two halves, the halves being displaced from each other by 3.06 mm. The prism can be tested with the aid of a gauge (fig. 5-a) consisting of two lines spaced 3.06 mm. from each other. This should produce the picture Figure 5-b.

The amount of displacement will be either correct or incorrect, but it cannot alter since

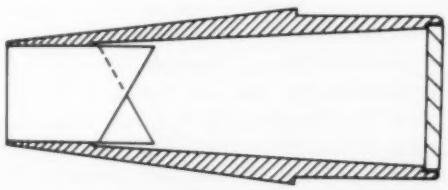

Fig. 4 (Schmidt). The prism of the Goldmann applanation tonometer.

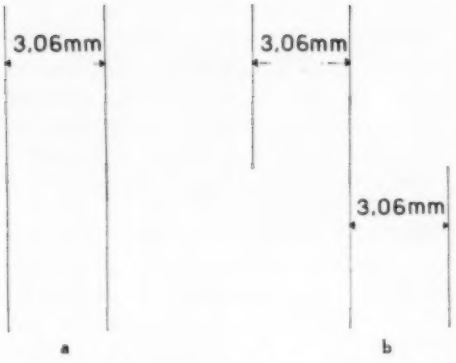

Fig. 5 (Schmidt). (a) Gage for checking the prism. (b) Diagram of appearance of gage seen through a correct prism.

the two prismatic surfaces are ground from a single piece of plastic. The manufacturers claim that the prismatic effect results in a dimension of 3.06 mm. with a tolerance of ± 0.05 mm. which may cause a maximum error of ± 3.0 percent. However, I can assure you that all prisms are made by one and the same worker and that the error is practically zero, as I have been able to confirm.

Now a description of the balance: the pressure is applied through a spring balance whose spring has been set and aged by 20,000 load reversals and in actual use is not stressed to its elastic limit. The performance can be checked with a reference weight (fig. 6) and any possible errors—with a load of 6.0 gm. an error of ±0.2 gm. or 2.0 mm. Hg is permissible—can be compensated with the aid of the correcting ring. One can see that the Goldmann applanation tonometer is really an accurate instrument. The outstanding feature of this applanation tonometer, compared with other types, is the great accuracy with which it measures very small areas and which also ensures that the difference between the P_o and P_t values is in fact insignificant.

The measuring process is carried out on the cornea with 10 times magnification of the microscope, thus eliminating parallax or magnification errors caused by changing accommodation effects on the part of the observer. Moreover, only one point of the cornea, the point at which the two semicircles intersect, is under observation. The measuring force is increased by rotating the measuring drum (figs. 2 and 6) until the semicircular borders of the flattened area of the cornea or the inner border of the fluorescein ring overlap (fig. 7). The circular area will then have a diameter of 3.06 mm. and the indicated pressure can be read off. It will be clear that accurate measurement of a very small area in applanation tonometry is made possible because only one measuring point has to be observed and this by a 10 times magnification of the microscope. This naturally leads to the question of whether even small surfaces can be effectively measured. A large area, involving a correspondingly larger volumetric displacement would of course result in a greater difference between the P_t and P_o values and the associated errors arising from variations on corneal

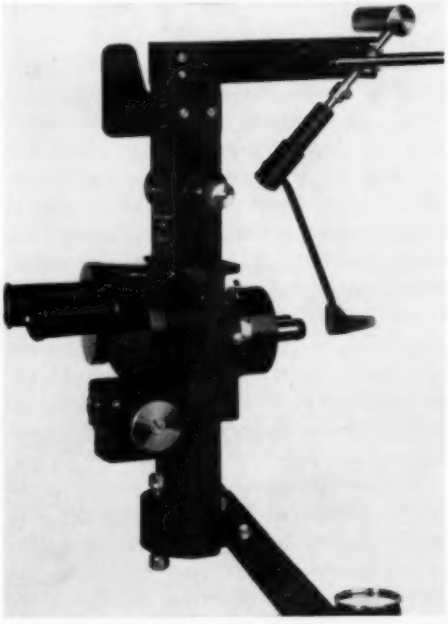

Fig. 6 (Schmidt). The reference weight mounted on the applanation tonometer.

curvature and ocular rigidity. Investigations with various applanation diameters have provided the results in Table 5.

The following P_t values were found in a patient, measurements being taken with a series of different applanation diameters, resulting in the corresponding "P_o" values after making due allowances for the volume and the ocular rigidity.

How is it that the P_t values corresponding to applanation diameters of less than 3.0 mm. are smaller than those corresponding to diameters greater than 3.0 mm. although the P_o values in this range with the larger flattened area are equal?

They are lower because the flattened surface of the Descemet's membrane, that is to say the inner surface of the cornea, is smaller than it should be in relation to the external flattened area. Under certain conditions, it is possible to measure the degree of flattening of the endothelium or the Descemet's membrane respectively and correct results may be expected if the ratio between the internal and external applanation areas is equal to the ratio between internal and external corneal radii. These conditions occur with an external applanation area of a diameter of approximately 3.0 mm.

For this reason no measurements should be made with diameters of less than 3.0 mm. while measurements with diameters of more than 3.5 mm. are subject to errors due to the larger volumetric displacement.

TABLE 5

RESULTS OF INVESTIGATION WITH VARIOUS APPLANATION DIAMETERS

Diameter of Applanated Area in mm.	P_t	"P_o"
2.0	18.0	18.0
2.5	20.0	19.8
3.0	21.6	21.0
3.5	22.1	21.0
4.0	22.8	21.0
4.5	23.9	21.0
5.0	25.7	21.0

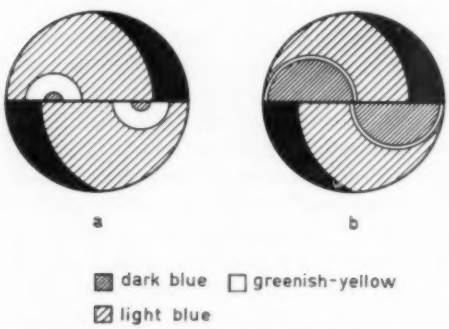

Fig. 7 (Schmidt). (a) Diagram of the appearance through the microscope when prism is in contact with the cornea and a small amount of force is applied. (b) When sufficient force is applied to flatten cornea to a diameter of 3.06 mm. at which time 1.0 gm. of force corresponds to 10 mm. Hg.

The reason for applanating a diameter of 3.06 mm. is that if a circle surface with this diameter is flattened one gm. of pressure corresponds to an intraocular pressure of 10 mm. Hg.

The great light intensity of the Haag-Streit slitlamp is another factor favoring measurements of such small flattened areas. The border of the flattened cornea is made visible by the action of blue light on the fluorescein; it is not really possible to work without stain. The unstained lacrimal fluid can be discerned in white light around the flattened area, but only the external boundaries of the band of fluid are visible as an illuminated line. It is, however, the inner boundary which is required for the measurement. In blue light, fluorescein takes on a greenish-yellow hue and thus provides an excellent color contrast against the blue background so that a clear line of demarcation can be easily recognized. Blue light is essential for this purpose, as fluorescein tends to give only a slight yellow coloring to the lacrimal fluid in white light. The outer boundary of the band of fluid is quite insignificant for measurement of the flattened area, owing to the fact that the width of the band changes from case to case.

It is most important to insure that a high-intensity slitlamp is used, since the blue

filter introduced into the light path absorbs all but a small amount of the emitted light. The angle between microscope and illumination should be as great as possible, so that the clear part of the prism is well illuminated and light is carried to the cornea. I am very often asked whether the applanation tonometer can be attached to this or that slitlamp: the answer to this is, that theoretically any slitlamp can be used, provided it is sufficiently bright.

Examination technique

The cornea is anesthetized with 0.2-percent Dorsocain solution (0.2-percent Novesin-Wander) one drop every five to 10 seconds for three doses. Both eyes should always be anesthetized to eliminate eyelid movement. The question arises whether anesthetics other than 0.2-percent Dorsocain (Dorsay) are also suitable for this purpose. I have tried to test other anesthetics and 29 different substances and concentrations were submitted to me. Unfortunately, there was not enough time available to test the suitability of every substance. I was, however, able to state that Pantocaine, Tetracaine and cocaine are unsuitable as they render the corneal surface liable to staining by fluorescein. Dr. Moses told me that Ophthaine works well. No measurements can be taken unless the corneal surface remains smooth and cannot be stained with fluorescein. I would specially recommend a 0.2-percent Dorsocain solution as this concentration does not in any way damage the corneal epithelium but nevertheless produces adequate anesthesia.

The lacrimal fluid is then stained with fluorescein paper. Only a few seconds are required to produce sufficient coloring. At the same time, I should like to point out that completely smooth fluorescein paper does not roughen the conjunctiva. Moreover, fluorescein crystals are more readily flushed off completely smooth paper. The head of the patient is then positioned in the head support and after cleaning the prism with 1:32,000 Merfen aqueous solution (that is a mercury compound of phenyl mercury borate) the pressure arm is swung into the path of the microscope and illumination. The blue filter is swung into position and the slit diaphragm is completely opened.

The operating voltage of the lamp is 6.0 v. or 7.5 v. if the lamp is somewhat aged. The microscope is set at 10 times magnification. I always use a magnifying power of 10 because the microscope with this magnification enables an intense brightness to be obtained while the great depth of focus provided in this way facilitates operation. The measuring drum is then set to approximately 1.0 gm. and the slitlamp is gradually advanced toward the eye of the patient.

It should be mentioned that one should start with 1.0 gm. because on the 0-position vibration of the prism on the cornea may result in acute discomfort to the patient.

The ophthalmic surgeon observes the prism from the side opposite the illuminator, along the microscope, until the prism just touches the cornea. This is indicated by illumination of the limbus. Before the prism actually touches the cornea, the pressure arm with the 1.0-gm. load will be located against the front stop. The distance between the front and rear stops is 2.0 mm.; on touching the cornea, the pressure arm will therefore be located within the desired measuring range. The progressive movement of the slitlamp is stopped as soon as the limbus is illuminated.

The patient must look straight ahead and in some cases the fixation light may be required to steady the eyes. The patient should also be asked to open the eyes wide. Should the patient have a tendency to close his eyes or to squeeze the eyelids as the slitlamp and the prism are advanced, he should be repeatedly urged to keep his eyes wide open. If there is still some danger of the eyelid or eyelashes coming into contact with the prism, the eyelids of the patient should be spread.

Once the patient has been irritated as the result of eyelids or eyelashes coming into contact with the prism, it will be very difficult to carry out any subsequent measurements.

Also, misleading results are obtained if eyelids or eyelashes are allowed to touch the prism. Conversely, if the patient feels nothing during the first examination he will be more inclined to keep his eyes wide open, without being urged to do so at subsequent examinations. The patient certainly feels nothing when the prism touches the cornea. At the moment of contact, he will merely see a diffuse, blue light.

If an eye is subjected to repeated measurements one after the other, it will be found (particularly in nervous patients, examined in this way for the first time) that the intraocular pressure is reduced, sometimes by several mm. Hg during the first minute. This cannot be due to a massage effect since a reduction of pressure due to such a cause from the P_t to the P_o value would only amount to a few 10ths of one mm. Hg. The reason is most probably a temporary increase of pressure due to fear of the measuring procedure. This drop in pressure is also noticed when using the Schiøtz tonometer if one minute is allowed to elapse between the first and second measurement.

A drop in pressure will also be noticed, if the prism is allowed to rest on the cornea while under measuring pressure. The reason for this phenomenon, which can also be observed in recently enucleated eyes under conditions of constant pressure, cannot therefore be due to a true reduction of the intraocular pressure, but to a nonelastic deformation of the cornea, which was described by Goldmann as "flowing." The thickness of the cornea is not maintained, and the external flattening no longer corresponds to the flattening of the membrane of Descemet. Only an apparent reduction of the intraocular pressure has therefore taken place.

Two rules can be deduced from these remarks:

First, the measurements must be repeated, perhaps in such a way that both eyes are measured alternately at brief intervals until the pressure is stabilized. This occurs after approximately one minute.

Secondly, the tonometer must not be allowed to remain in permanent contact with the cornea at measuring pressure for more than half a minute.

There are other reasons why measurement of an eye should not take more than one minute: extended measurement of one eye leads to more or less pronounced drying of the corneal epithelium of both eyes. A fluorescein-stained ring is formed around the point of contact of the cornea and prism of the eye under investigation. In the other eye, fluorescein-staining areas of irregular shape are formed which render all reliable measurements quite impossible. The actual measuring procedure should therefore be as brief as possible and should be applied alternately to both eyes. The ring-shaped stain does not inconvenience the patient because the measurement is carried out in the center of the cornea which is free of stain. Even extensive drying effects vanish after a short time without any treatment. The vision is of course temporarily slightly affected; however, for a very short time. Examinations to determine the visual acuity and visual field should therefore be carried out prior to tonometric tests.

I should like to stress one very important point:

Immediately after the prism has touched the cornea, the microscope must be accurately focused so that the inner border of the fluorescein ring can be seen with optimum sharpness. The important inner border of the fluorescein ring is not seen quite as distinctly as the sharply bordered outer edge owing to the fact that the thickness of the band diminishes toward the area of contact.

A method enabling the correct result to be obtained from one measurement in the case of corneal astigmatism is included in the operating instructions. Frequent references to this method may create the impression that this is extremely important. Astigmatism of the cornea of more than three diopters may affect the results with a smaller or greater error. However, astigmatism exceeding three

diopters is comparatively uncommon and it is best to ignore astigmatism when first practicing applanation tonometry. Only when sufficient familiarity with the instrument has been acquired should the errors resulting from severe astigmatism be eliminated. It is quite clear that tonometric measurements involving a constant small area represent an ideal method and that the Goldmann applanation tonometer is a simple and accurate instrument; however, a number of important points have to be observed if reliable results are to be obtained. Satisfaction with the new tonometer will be achieved as soon as manipulation of the slitlamp becomes automatic.

In which cases may one expect incorrect result?

In all cases involving extensive changes of the cornea, lesions of the epithelium, corneal injuries, corneal inflammation, extensive corneal scars and growths. It may be possible to carry out measurements in these conditions but the result must be evaluated with caution. This also applies to tests carried out with the Schiøtz tonometer in such cases. The measured values can, however, be accepted without question in cases of microcornea and megalocornea while the Schiøtz tonometer used in conjunction with the usual calibration tables would almost certainly provide the wrong results.

What limiting values of the intraocular pressure are found with the applanation tonometer? About 99 percent of normal intraocular pressures are less than 22 mm. Hg. A somewhat smaller dispersion area than in the Schiøtz tonometer must be expected in any case, since the rigidity and the corneal radius do not affect the accuracy of the measured result, while the inherent error of the instrument is only approximately $\pm$ 0.5 mm. Hg. Each individual measurement with the Schiøtz tonometer is of course subject to an error of $\pm$ 1.0 scale division (Küchle and Rohrschneider). The normal pressure has a mean value of 15.5 mm. Hg ($\pm$2.5 mm. Hg = standard deviation).

This brings us to the question of the type of patient on whom we perform applanation tonometry in our clinic. These include all patients of more than 40 years of age and all myopic patients of more than 20 years of age if myopia amounts to more than three diopters.

Although we know the distribution of pressure among the general population, we do not know this distribution among those suffering from glaucoma. We must assume that the distribution curves of normal persons and those suffering from glaucoma overlap to some extent, that is to say, there are glaucoma patients with normal intraocular pressure. We have therefore taken 21.0 mm. Hg, or the mean value plus 2.0σ (= 95 percent of the normal) as the limiting value for our purpose and regard higher values as suspect of glaucoma, that is, we subject these people to further investigations.

It may be possible that one or the other glaucoma patient will not be detected in this way, but I believe the number of undetected patients to be very small indeed.

If the pressure is less than 21 mm. Hg and neither the papillary condition nor case history and chamber depth point to the presence of simple or acute glaucoma, no further tests are made to detect glaucoma. If the pressure exceeds 21 mm. Hg, the visual field is tested on another day and at the same time tonometry is repeated. If the pressure does not exceed 22 mm. Hg at any time, and if the visual field is normal, a re-examination of visual field and intraocular pressure is fixed for one year after the initial examination. If the patient does not attend on his own initiative within 13 months, he is reminded twice by letter. This assumes that a glaucoma file is maintained which includes all patients with an intraocular pressure of 21 mm. Hg and more.

With intraocular pressure between 22 and 24 mm. Hg, the tonometer test is repeated after eight days and the visual field is tested after six months provided it was normal at the first examination.

Even with slight changes of visual field

and intraocular pressures of less than 24 mm. Hg or with a normal field and pressures exceeding 24 mm. Hg, it is strongly recommended that whenever possible, a diurnal pressure curve be plotted, either on an in-patient or out-patient basis. The patient should continue with his normal mode of life and should attend the clinic at 4:00 P.M. and 8:00 A.M. to enable the pressure to be checked. On one or two occasions, the patient sleeps overnight in the clinic so that the intraocular pressure can be measured in the dark with the Schiøtz tonometer at about 7:00 A.M. An hour later, at 8:00 A.M., the pressure is again measured with both the Schiøtz and the applanation tonometer. The difference between the values obtained with the Schiøtz tonometer, and the applanation tonometer is a measure for the rigidity of the eye, this value being practically constant over a wide measuring range, Surgery, however, may change the scleral rigidity. The mean of the difference values (which are determined three times) can be used to correct the Schiøtz results without difficulty, thus enabling the correct P_o value to be established. The difference values are particularly useful if an applanation tonometer is not always available. It is, however, essential that the same Schiøtz tonometer is used with which the difference values were established in the first place.

If the pressure curves show several peaks higher than 23 mm. Hg or more, therapy is started by administering one drop of Pilocarpin in the evening. The pressure may be considered as stabilized when it remains below 20 mm. Hg continuously for at least two days. Control checks are made after eight days and subsequently after 14 days. Medical therapy is also started if a pressure of less than 22.5 mm. Hg is measured continuously where this is accompanied by a deterioration of visual field. A change of medical therapy with a diurnal pressure curve is ordered if the pressure exceeds 23 mm. Hg several times, or if the visual field deteriorates while the pressure remains below 22.5 mm. Hg. The pressure level is lowered by at least 2.0 mm. Hg if a deterioration of visual field is detected under conditions of normal pressure.

Surgical treatment must be resorted to if the pressure is constantly greater than 26 mm. Hg despite optimum medical therapy or in the event of deterioration of the visual field accompanied by a pressure of between 22 and 26 mm. Hg which is not affected by medical therapy. If the pressure is stabilized below 20 mm. Hg, the visual field is checked every four months, or every two months if the pressure has some value between 20 and 22 mm. Hg.

Gonioscopic examinations are of course also carried out while the diurnal pressure curve is plotted. Provocative tests, as the so-called water-drinking test, are only made if the result of the perimetry indicates glaucoma despite normal pressure conditions as recorded in the diurnal pressure curve. There are many clinics in Europe which carry out far more frequent examinations, numerous provocative tests, and prolonged diurnal pressure recordings in their treatment of glaucoma patients. However, we believe that, for the time being, our plan of treatment insures optimum facilities for glaucoma patients.

University of Bern.

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DISCISSION WITH THE AID OF A FIXATION NEEDLE (SATO TECHNIQUE)*

TSUYOSHI YAMASHITA, M.D., AND ROBERT C. DREWS, M.D.
Saint Louis, Missouri

Few surgical techniques seem so simple and can prove so frustrating as discission, especially of certain secondary membranes. When discission is finally accomplished it is too often with distortion of the globe, traction on the ciliary body, and vitreous disruption.

Bowman[1] pointed out that "if two needles are brought to bear on the opaque capsule from different sides of the cornea or sclerotica, each furnishes the other with a point of resistance, and the capsule may be torn or cut at pleasure, in almost any direction, and generally without any drag on the neighboring vascular structures." The co-ordinated ambidexterity required by Bowman's technique has prevented its greater use.

SATO TECHNIQUE

In 1951, Tutomu Sato described a technique for discission of secondary membranes in which a fixation needle was used.[2] This instrument is essentially a needle-knife with a handle that is only about a half-inch long and a curved chisel-like blade. While the fixation needle stabilizes the membrane, discission is made with a specially designed needle-knife having an angled blade (Sato knife).

With maximum pupillary dilatation, the fixation needle is introduced obliquely into the anterior chamber through the cornea at a point just anterior to the limbus (fig. 1). The fixation needle is advanced to the membrane at the nearest pupillary margin and, with a slight upward pricking motion, the membrane is both pierced and lifted from the vitreous face. The needle is then advanced between the membrane and the vitreous face piercing the membrane again at the opposite pupillary margin. The entire membrane is now tented forward slightly, and the fixation needle is thrust through the sclera just behind the limbus. With this double transfixion of both the wall of the anterior chamber and the membrane, the surgeon no longer needs to hold the fixation needle and is free to devote all his skill to maneuvering the needle-knife.

The Sato knife is now introduced obliquely through the cornea just distal and posterior to the fixation needle. The membrane is incised with strokes in the horizontal (frontal) plane, against the posterior edge of the fixation needle. The fixation needle provides the much needed support against which to cut, and the avoidance of vertical (corneal and sagittal) strokes with the knife helps to prevent incision of the vitreous face. The angled design of the Sato blade proves to be a great aid in directing the cutting strokes. With rotation of the handle it is possible to lift and cut the membrane at the same time.

These basic techniques can be altered and extended as needed. The entwining of a strandlike membrane on the fixation needle, iris sphincterotomy in cases with posterior

* From the Department of Ophthalmology and the Oscar Johnson Institute, Washington University School of Medicine. This investigation was supported in part by a research grant to the Department of Ophthalmology from Mrs. Edgar M. Queeny.

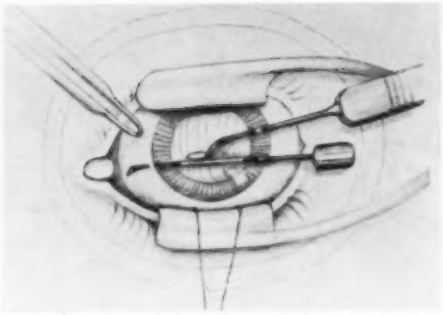

Fig. 1 (Yamashita and Drews). *Surgeon's view.* The globe is stabilized with forceps and a superior rectus suture. The fixation needle transfixes both the cornea and the pupillary membrane, which is then incised with horizontal strokes of the angled Sato knife, avoiding the vitreous face if possible.

synechias or updrawn pupil, optical iridotomy, multiple incisions, and other modifications may need to be devised in certain cases. The use of Sato's instruments allows a wider range for solution of these special problems[3] (fig. 2).

Clinical Experience

We have used these instruments* in 24 operations at this time (table 1). The marked superiority of a technique which allows stabilization of a membrane, the iris, or the tough membranous anterior capsule of a lens with secondary anterior polar cataract, and so on, becomes even more obvious in practice than in theory.

Is it really possible to lift secondary membranes free of the vitreous face and incise them without injuring the vitreous? Obviously not in cases where the opacity is of the vitreous face itself or involves the anterior layers of the vitreous. In the 16 eyes where we tried to avoid the vitreous we were successful in 12 cases. One of these showed a spontaneous rupture of the vitreous face later anyway. At a time when retinal detachment is thought to be frequently associated with pathologic conditions of the vitreous, and when some patients may be candidates for future anterior chamber lens implants, the preservation of the vitreous face may become more than just physiologic.

Whether a better opening can be obtained with this method is a matter of opinion. On the basis of experience we feel that a good opening can be obtained with less trauma; in some instances, with very much less trauma. For the conservative surgeon this may make the difference between an excellent opening and none at all.

The method is not advocated as a substitute for surgical skill. Indeed, more ingenuity and dexterity is certainly required for its best application than the more straightforward, brute-force techniques sometimes

* The Sato instruments are available from Inami Medical Instruments Co., 8, 1-Chome, Asakusabashi, Taitoku, Tokyo, Japan, and the Storz Instrument Company, 4570 Audubon, Saint Louis 10, Missouri.

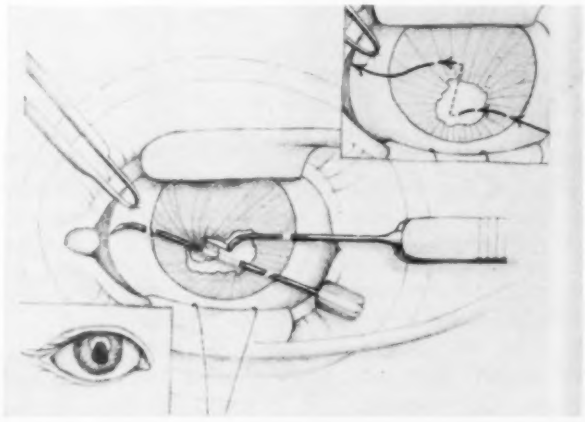

Fig. 2 (Yamashita and Drews). (Insert upper right) *Surgeon's view.* The arrows show the path to be taken by the fixation needle to prepare for a combined iris sphincterotomy and membrane incision in a case with an updrawn pupil.

(Central figure) *Surgeon's view.* The incision is made avoiding the vitreous face. Note that the devious route taken by the fixation needle has resulted in a twisting of the iris-membrane diaphragm to allow a vertical opening to be made with the knife in the more accessible horizontal position.

(Insert lower left) Postoperatively the pupil is centrally placed.

TABLE I

SATO TECHNIQUE: CLINICAL EXPERIENCE

Patient	Age (yr.)	Diagnosis*	Operation	Result		Vitreous Face
R. M.	54	1	Discission	20/200	20/25	Incised
K. A.	79	2	Discission	20/200	20/30	Intact
B. A.	67	2, 11	Discission	20/70	20/40	Broken
R. S.	55	2	Discission	20/100	20/40	Intact
H. W.	76	2, 11	Discission	20/70	20/50	Broken
L. L.	76	2, 10, 11	Discission	H.M.	20/60	—
H. L.	37	4	Discission	20/200	20/70	Broken
B. M.	80	2, 9, 10	Discission and iris sphincterotomy	20/200	20/40	—
T. M.	72	1, 12	Discission and iris sphincterotomy	20/100	20/50	Intact
				Bombé relieved		
O. W.	75	2, 9, 11, 12	Discission and iris sphincterotomy	20/200	20/100	Intact
				Bombé relieved		
T. J.	14	2, 9	Iridotomy	H.M.	20/100	Intact
				Good pupil with membrane behind		
P. F.	61	2, 11	Discission	H.M.	20/100	Intact
M. Y.	57	2	Discission	20/200	20/40	Intact
A. G.	28	2	Discission	20/50	20/25	Intact
L. B.	10	3	Discission	20/70	20/20	Intact
N. R.	13	8, 13, 14	Discission and iris sphincterotomy	10/200	10/200	Intact
				Good opening		
H. M.	71	2	Discission	10/200	20/40	Incised
J. H.	9	7	Discission	20/100	20/25	Incised
J. L.	75	9, 10	Iris sphincterotomy	20/100	20/100	—
				Reading improved		
P. D.	10	3, 13	Discission	20/200	20/20	Broken
W. H.	10	6	Discission	Very poor	J3	Incised
D. H.	15	5, 15	Discission	20/100	20/50	Incised
D. O.	1	5	Discission	Good opening		Intact
S. S.	5	5, 14, 16	Discission	Good opening temporarily		Intact

* DIAGNOSES

1. Inflammatory membrane after an intracapsular cataract extraction.
2. Secondary membrane after an extracapsular cataract extraction.
3. Secondary membrane after Barkan lavage of a traumatic cataract.
4. Secondary membrane after Barkan removal of a congenital cataract.
5. Secondary membrane after needling and lavage of a congenital cataract.
6. Secondary membrane after combined extraction of a congenital cataract
7. Secondary membrane after needling a congenital cataract.
8. Cyclitic membrane after multiple needlings of a congenital cataract.
9. Updrawn pupil.
10. Vitreous loss complicating the cataract extraction.
11. Macular degeneration.
12. Posterior synechia with iris bombé.
13. Glaucoma.
14. Nystagmus.
15. High myopia.
16. Microphthalmos.

required with a single needle-knife.

Although we have had no experience with it, we would suggest that the Sato fixation needle would be ideal for trapping dislocated lenses in the anterior chamber since the surgeon does not need to continue to hold the handle of the instrument.

SUMMARY

On the basis of our experience in 24 cases in which the Sato fixation needle and Sato needle-knife were used in combination for discission, we would strongly recommend the adoption of the technique as easier, more effective, and attended by less trauma to neighboring structures than single needle-knife techniques. It requires less skill and affords greater freedom of action than a double needle-knife technique.

640 South Kingshighway (10).

ACKNOWLEDGMENT

We would like to thank Miss Pearl Drews for making the illustrations used in this paper.

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GLAUCOMA OF MYOPIC INDIVIDUALS AND ITS OPERATION*

GYULA LUGOSSY, M.D.
Budapest, Hungary

In this paper the attention of practitioners and of physicians working in out-patient clinics should be drawn to a rather neglected field in the fight against blindness. The glaucoma of the myopic is rarely discussed in textbooks, manuals, or at scientific sessions. Weinstein states that, according to general opinion (Cori, Gala, Kraupa, and others), the majority of patients suffering from glaucoma and an anomaly of refraction are hypermetropic. In his material, refraction was determined in 1,459 of 3,214 glaucoma cases. He found emmetropia in 23 percent, hypermetropia in 62 percent, and myopia in 15 percent.

From this point of view, the examinations of Hruby are rather interesting. After studying the data related to the conditions of refraction in the entire population, he found that emmetropia, hypermetropia, and myopia display much the same distribution among the healthy and the glaucomatous individuals. Thus, it is unlikely that myopic individuals have a weaker predisposition to glaucoma, the fact being that myopic individuals are in a minority.

Weinstein also quotes Löhlein who found that myopia is a frequent condition among the young glaucomatous patients. As an explanation he claims that in the young, axis myopia develops as a sequel of increased intraocular pressure; both conditions may be inherited. Further, Weinstein emphasizes the fact that congestive glaucoma is more frequent in hypermetropic eyes, while myopic ones are mostly affected by glaucoma simplex.

It is well-known that, parallel with age, the lens becomes swollen and its convexity increases; emmetropic eyes thereby may become gradually myopic. This kind of myopia will not be discussed, only the glaucoma arising in primarily myopic eyes will be dealt with. The glaucoma of these individuals may cause much diagnostic difficulty if the examination of the fundi is hindered by phakosclerosis. Myopia and blurred lenses in a patient constitute a pitfall for the ophthalmologist who is likely to ascribe the deterioration of sight to the two manifest morbid conditions. In the meantime, the unrecognized glaucoma progresses to the stage where its diagnosis may be too late. The cases to be reported in detail are evidence for this statement.

CASE REPORTS

CASE 1

M. L., a 56-year-old man, has vision of: R.E., with a −6.5D. sph. ⊃ −0.5D. cyl. ax. 90°, 5/10; L.E., with a −7.0D. sph. ⊃ −1.5D. cyl. ax. 170°, 5/10. Episcleral congestion was present; normal angle of chamber; clear refracting media. Fundus was pale-gray; funnel-shaped papilla. Considerable contraction of the visual fields. Markedly increased intraocular pressure (fig. 1). Blaskovics' operation, cyclodialysis inversa duplex, was performed at the superior rectus muscle, on both eyes, at different times. Normal tension resulted from the operation.

Comment. The ophthalmologist who examined the patient for the correction of his myopic astigmatism neglected the examination of the fundus. It was due to this fact that the operation was carried out at a time when severe contraction of the visual field

* From the Department of Ophthalmology, State Institute of Rheumatology and Balneology.

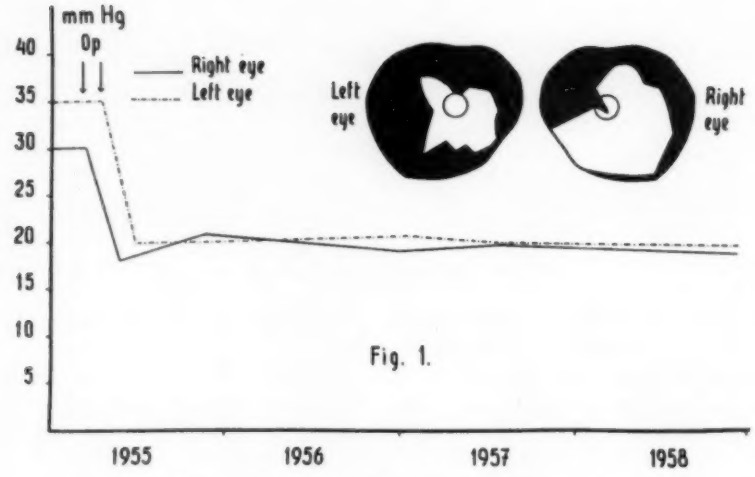

Fig. 1 (Lugossy). *Case 1.* Markedly increased intraocular pressure.

had already ensued. The deterioration of the sight would not have ensued if the previous examinations had been done with proper care.

CASE 2

A. J., a 61-year-old man, was admitted for a cataract operation. Vision was: R.E., counting fingers at 0.5 m., no correction possible; L.E., counting fingers at 1.0 m., with a —9.0D. sph., 5/25. Intracapsular cataract extraction with round pupil was performed on the right eye. On the 10th postoperative day the aphakic correction was: +8.0D. sph. ⊃ +2.0D. cyl. ax. 170°, with a very eccentric oblique position of the head, hardly resulted in vision of 5/15, instead of the expected 5/5.

Ophthalmoscopy revealed a pale, deeply excavated papilla. The visual field was considerably contracted (fig. 2). In the left eye the chamber was intact; there were phakosclerosis, a slight excavation of the papilla, and a slight nasal contraction of the visual field. On the intraocular pressure curve, there were tiny eminences above the normal upper limit. The contraction of the left visual field exhibited some worsening over a year, so Blaskovics cyclodialysis inversa was done at the superior rectus

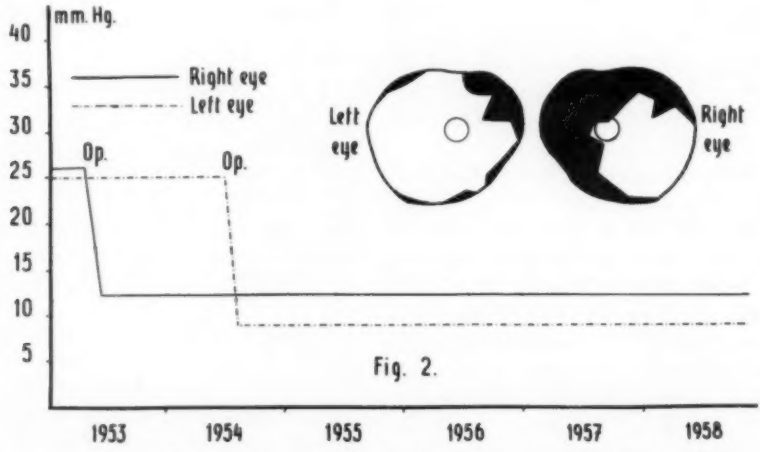

Fig. 2 (Lugossy). *Case 2.* Note markedly contracted visual field.

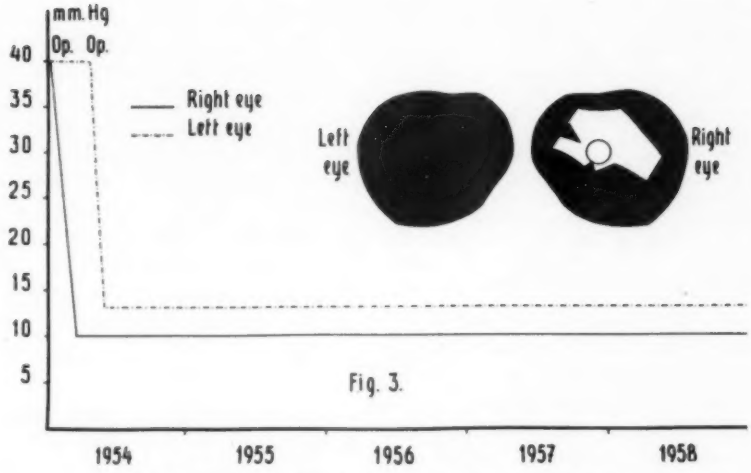

Fig. 3 (Lugossy). *Case 3.* Visual field and tension studies.

muscle. The eye has become hypotonic. The visual field is unchanged. Vision is, —11D. sph., 5/40. He reads, at 10 cm. distance, test types IV without glasses.

Comment. In the presence of myopia and cataract, the glaucoma simplex of the patient had not been discovered; therefore, the successful operation for the cataract was carried out on an eye that was practically of no use. Still, the hospitalization was useful because the glaucoma of the other eye was detected and the eye was operated on in time; removal of the cataract from this eye will not be useless.

CASE 3

G. B., a 68-year-old woman, was admitted for thorough examination. Her sight had, in recent

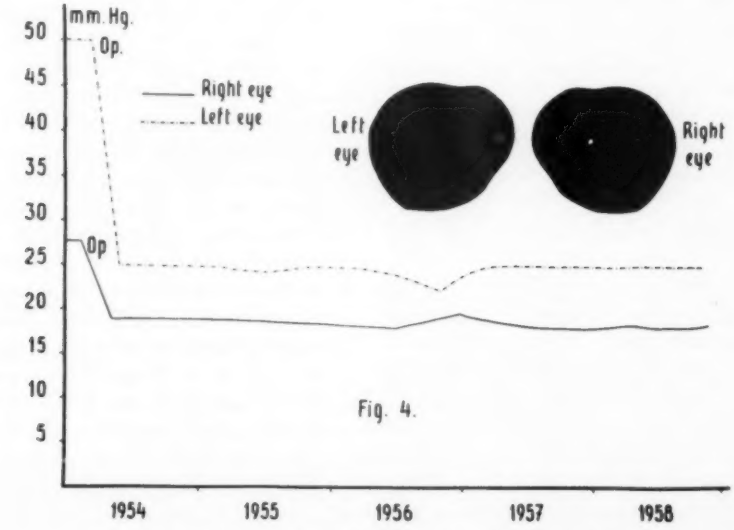

Fig. 4 (Lugossy). *Case 4.* Visual fields could not be taken.

years, become gradually worse, and glasses brought no improvement. Vision was: R.E., with a 10D. sph., 5/12; L.E., —10D. sph., counting fingers at 1.5 m. She had intact chambers, medium wide pupils, and phakosclerosis which was more progressed on the left side. The right papilla was slightly, the left one markedly, pale and excavated. Tension was: R.E., 40; L.E., 40 mm. Hg. The right visual field was contracted, the left could not be outlined (fig. 3). Cyclodialysis inversa duplex was performed on the right eye at the superior rectus muscle. Since then, the tension has been low. The cataract of the left eye was extracted in intact capsule after a broad iridectomy, but the sight has not improved.

Comment. The glaucoma simplex of the myopic patient was not discovered, although during the course of many years glasses were repeatedly prescribed for her. Therefore, her left eye was practically blind when she was thoroughly examined. In the right eye, contraction of the visual field, associated with myopia and cataract, was additional evidence of deterioration of sight. Hospitalization prevented the blindness of this right eye.

CASE 4

S. G., a 74-year-old man, was admitted for cataract operation. He had had poor sight for years, especially in the left eye. One year before the present admission pilocarpine was prescribed for him to use "at pleasure." Each drop was followed by dimmed vision, after six months of irregular application, he omitted its use.

Vision was: R.E., counting fingers from a few cm. only, no correction is possible; L.E., light perception only. Episcleral congestion, intact chambers, atrophic spots on the iris, wide, round pupils, with nearly no reaction to light on the left, were found. The phakosclerosis was more progressed on the right than on the left. Fundi were pale-gray, with excavated papillae surrounded by a ring-shaped atrophy of the choroid. Visual fields could not be taken. Tension was: R.E., 26; L.E. 50 mm. Hg. After instillation of two-percent pilocarpine solution (R.E., three times a day; L.E., five times, tension was: R.E., 18; L.E., 26 mm. Hg) (fig. 4). In the right eye a total iridectomy and intracapsular cataract extraction were carried out, with the result that he counts fingers from one m. According to earlier findings the patient could read, two years ago, test types VII with the right eye, test types VI with the left eye, from 15 cm. No doubt, the operation would have brought about a better result, if he had used pilocarpine regularly.

Comment. The chronic glaucoma affecting the myopic and phakosclerotic eye was duly recognized by the ophthalmologist who prescribed glasses for the patient. However, he did not inform the patient about the significance of systematic instillations as well as the blurring of vision attending miosis. Therefore, the patient, not being informed that instillation is followed by the contraction of the pupil which causes blurred vision, drew the erroneous conclusion that his sight would improve if he does not apply drops. The extreme deterioration of sight could have been prevented if there had been greater confidence between physician and patient.

CONCLUSIONS

The reported cases demonstrate that in myopic patients the cause of poor sight should be thoroughly investigated when they are examined for eyeglasses. Special care is imperative in cases in which the vision cannot be fully corrected with lenses. Not infrequently dimness of sight due to phakosclerosis gives rise to misinterpretation of the condition, and the real cause of poor vision, the glaucoma, remains undiscovered. Thus, the possibility of glaucoma should always be considered in the presence of myopia. Blindness, the tragic sequel of diagnostic errors, cannot be prevented unless all patients are carefully examined, including ophthalmoscopy.

SUMMARY

On the basis of four records I point out that the recognition of glaucoma may be readily missed in myopic patients. The examination of the fundus is, during refraction, frequently difficult because of a dim vision in the center of the crystalline lens. When the causes of visual deterioration are sought, glaucoma should be taken into consideration, as well as myopia and cataract. In cases of glaucoma discovered too late or not at all, removal of a cataract is of little or no use as far as improving sight is concerned. If the glaucoma is discovered in time, the patient should be informed about the effect of pilocarpine, so that he will not neglect instillation.

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NERVOUS MECHANISMS FOR THE CONTROL OF INTRAOCULAR PRESSURE*

MILES A. GALIN, M.D.
New York

That the intraocular pressure in any given normal eye varies within well-defined boundaries is well known. However, the mechanism of this rather rigid homeostatis is not well understood. Perkins[1] has outlined the theoretic factors that might be applicable. These include capillary pressure, rate of aqueous secretion, nature (osmolality) of aqueous, and outflow resistance, including episcleral venous pressure.

Of the mechanisms that might be available to inter-relate these factors, nervous control has received the most attention. Vascular and humoral factors, which have been studied,[2,3] may also reflect changes in innervation.

To investigate the effect of sensory pathways on the intact human eye, therefore, is desirable. One factor that readily lends itself to study is the ocular consensual response. Tonography, for example, performed on one eye leads to a reduction in intraocular pressure in the contralateral eye, apparently without alteration in outflow facility.[4,5] Tonography performed on patients without fifth-nerve function would permit assessment of that nerve's function on the ocular consensual response.

The nature of "intraocular pressure readjustment" after Diamox administration would also be of interest in this special group of patients. It has been reported[6] that the facility of aqueous outflow is reduced, presumably as a compensatory measure, after the intraocular pressure has been lowered by Diamox administration. It was thought that some insight into the mechanism of this phenomenon might be gleaned from studies of the Diamox effect on fifth-nerve denervated eyes.

MATERIALS AND METHODS

Six patients who had undergone retrogasserian neurectomy for idiopathic tic doleureux were studied. All patients had total corneal anesthesia and operative evidence of complete section. No ocular or neurologic deficit, except for sensory loss, was present.

Tonography was performed on several occasions until the patients became used to the procedure. Results, after acclimatization, were quite uniform. Tensions were recorded in both eyes and tonography performed on one eye. Immediately after completion of tonography (four minutes), tensions were taken in the contralateral eye. Both eyes were studied in this manner on a minimum of two occasions. The Mueller electronic tonometer was used for all readings and the 1955 tables employed. It is believed that this tonometer can be read to 0.25 scale units with a fair degree of accuracy in the ranges studied. Control patients were handled similarly.

* From the Department of Surgery (Ophthalmology), of The New York Hospital-Cornell Medical Center. Aided in part by a grant from The National Council to Combat Blindness.

In the Diamox study, 500 mg. of Diamox were administered intravenously two hours after tonography had been performed on the involved eye. Thirty to 45 minutes after Diamox administration, tonography was repeated. Control patients, as well as the normal eye, were handled similarly.

Results

Table 1, which summarizes the results of the ocular consensual study, shows that all patients exhibited a consistent consensual response regardless of which eye was stimulated. Though the magnitudes of pressure changes were small, they were essentially similar and quite reproducible.

No consistent results could be obtained in the Diamox study in either control or experimental patients. Though Diamox reduced intraocular pressure in all patients, alterations in the facility of aqueous outflow were either negligible or not reproducible. Consequently, the data from the experimental group have little meaning and have not been included.

Discussion

The effect of the fifth nerve on ocular homeostasis has been studied in great detail. Hartmann[7] investigated the effects of retrogasserian neurectomy in man and concluded that no fibers regulating ocular tension were carried with the fifth nerve.

Perkins, in detailed rabbit studies, demonstrated immediate effects on the ipsilateral and contralateral eyes when the intact fifth nerve was stimulated mechanically. On the ipsilateral side, pupillary contraction, a rise in temperature of the ciliary region, increase in intraocular pressure, and increased aqueous protein resulted. In 15 percent of the animals, consensual increase in intraocular pressure occurred. In 50 percent of experiments increased aqueous protein was noted in the contralateral eye. Perkins further reported that in rabbits, the fifth cranial nerve can mediate impulses for raising the intraocular pressure, though perhaps this might not occur in the normal control of intraocular pressure.

Somewhat similar conclusions were reached by von Sallmann in his study of cats and monkeys.[8]

The results of the present study would tend to indicate that whatever the mechanism governing the ophthalmic consensual response may be, it does not depend upon the integrity of the fifth nerve. Furthermore, no abnormalities in the regulation of intraocular pressure have been noted in these patients. All patients in the group were also subjected to detailed provocative testing,[9] and demon-

TABLE 1

OCULAR CONSENSUAL RESPONSE TO TONOGRAPHY IN NORMAL AND FIFTH-NERVE DENERVATED EYES

Patient	Intraocular Pressure in Undisturbed Anesthetic Eye (mm.Hg)	Intraocular Pressure in Undisturbed Normal Eye (mm.Hg)	Facility of Aqueous Outflow in Anesthetic Eye	Immediate Intraocular Pressure in Normal Eye after Tonography in Anesthetic Eye (mm.Hg)	Facility of Aqueous Outflow in Normal Eye	Immediate Intraocular Pressure in Anesthetic Eye after Tonography in Normal Eye (mm.Hg)
Controls (average of all patients)	13.0	12.75	0.31	11.4	0.33	12.0
E. B. (average of 5 runs)	12.0	12.0	0.25	10.4	0.30	10.8
M. M. (average of 4 runs)	16.0	17.0	0.30	15.0	0.30	14.4
B. C. (average of 6 runs)	13.0	14.0	0.25	12.5	0.20	11.8
M. L. (average of 3 runs)	15.0	16.0	0.25	14.3	0.32	13.2
S. H. (average of 2 runs)	11.0	12.0	0.22	10.1	0.28	10.0
J. M. (average of 4 runs)	17.0	18.5	0.34	16.8	0.36	15.4

strated no abnormalities. This would not be the case if the fifth nerve had a major regulatory function.

It would be convenient to explain the maintenance of intraocular pressure by relegating it to a system in which the afferent arc responds to alterations in pressure and initiates the response that ultimately leads to alteration in outflow facility, aqueous inflow, blood flow, and so forth, until normalcy is restored. No real evidence that the fifth nerve serves such a function has yet appeared in the literature, and this study would, in part, tend to controvert such a supposition.

SUMMARY

The ophthalmic consensual response is intact in patients who have undergone retrogasserian neurectomy. It is suggested that the fifth nerve does not play a major role in the homeostatic mechanism for the maintenance of intraocular pressure.

525 East 68th Street (21)

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SYSTEMIC HISTIOCYTOSIS*

WITH INTRAOCULAR INVOLVEMENT: REPORT OF A CASE

HENRY J. KINOSIAN, M.D.
Ogdensburg, New York

Buphthalmos due to infiltration of the iris, ciliary body, and trabecular meshwork with histiocytes has been reported in cases of nevoxantho-endothelioma,[4-6, 8] but no case of systemic histiocytosis with similar ocular involvement has appeared in the literature. It is the purpose of this report to consider the classification of the histiocytic diseases and to describe such a case.

Histiocytes (macrophages) are derived from the monocytes of the blood and from the fixed tissue macrophages of the reticuloendothelial system.[1] They appear in response to inflammation, and their function is phagocytic, for example, if they ingest dead or dying cells they have the appearance of a multinucleated cell, and if the ingested material is lipid, they appear as foam cells. Lichtenstein[2] suggested the term histiocytosis X to include all cases of generalized histiocytosis which had previously been classified as eosinophilic granuloma of bone, Hand-Schüller-Christian disease, or Letterer-Siwe disease, for he felt

* From the Department of Surgery (Ophthalmology) of The New York Hospital-Cornell Medical Center.

they were all clinical variants of the same disease entity. It is well known that patients in this group develop cutaneous xanthomas which are clinically and histologically similar to those classified as xanthoma disseminatum. For this reason Crocker[3] grouped them together in his classification of the cutaneous xanthomas of childhood:

Type I.: Serum cholesterol (and fats) normal
Group A: Xanthoma disseminatum (including those originally called "naevo-xanthoendothelioma" and juvenile xanthoma)
Group B.: Xanthomas accompanying various chronic diseases, especially the "eosinophilic granuloma syndromes," or the so-called "reticulo-endothelioses" (including Hand-Schüller-Christian disease and Letterer-Siwe's disease)
Type II.: Serum cholesterol (and fats) elevated
Group C.: Xanthoma tuberosum (including essential familial hypercholesterolemia)
Group D.: Secondary or eruptive xanthomas (including the transitory xanthomas of diabetes mellitus, idiopathic familial hyperlipemia, nephrotic syndrome, hypothyroidism, obstructive liver disease and von Gierke's disease).

Crocker points out that the diagnosis of a xanthoma of Type I as "xanthoma disseminatum" is largely one of exclusion after the generalized xanthomatoses (histiocytosis X of Lichtenstein) have been ruled out. However, the prognosis in the former is excellent, since there is usually a slow spontaneous regression of the lesions.

Lichtenstein classifies the histiocytoses according to the clinical manifestations:

Histiocytosis X: Localized to bone (eosinophilic granuloma, solitary or multiple)
Histiocytosis X: Disseminated or acute (L-S syndrome), with destructive skeletal lesions (E-G), with transition to the chronic phase (S-C)
Histiocytosis X: Disseminated, chronic (S-C syndrome), with destructive skeletal lesions (E-G), with early extraskeletal sites resembling E-G, with acute or subacute exacerbation (L-S), with involvement of bones, lungs, pituitary, and/or brain, skin, mucosa (oral, anal and genital), liver or lymph nodes (in varying combinations as the case may be).

This classification takes into account the transitions between the clinical forms of the disease observed in patients. Lichtenstein cites a case of an otherwise healthy child, aged three years, who first presented with multiple skeletal lesions. A diagnosis of eosinophilic granuloma of bone was made on bone biopsy. After some months acceleration of the disease was noted and the child presented with the Hand-Schüller-Christian form and finally died from the acute form of the disease with many fresh skeletal and visceral lesions. Generally, the prognosis of histiocytosis X localized to bone is good, with cure being frequently effected. For the acute or subacute forms (Letterer-Siwe syndrome), the disease is probably not invariably fatal, for it may enter the chronic phase (Hand-Schüller-Christian syndrome) where the prognosis is guarded. Transitions between these forms of the disease may occur in a patient, thereby altering the prognosis.

The first report of systemic involvement in a case of nevoxantho-endothelioma was made by Blank,[4] who described a Negro child, aged four months, who presented with photophobia and an apparent mass in the iris thought to be a sarcoma. For this reason the eye was enucleated. Four months later skin lesions developed. He was admitted, and the biopsy of the skin lesions showed massive infiltration of the corium by "nevuslike" cells, which are probably identical with histiocytes with giant cell formation. The eye was normal except for the iris and ciliary body, which were infiltrated by "nevuslike" cellular proliferation. These were identical with those cells of the skin lesions. Giant cells were also present within the iris.

Maumenee's case[5] also demonstrated infiltration of the iris, ciliary body and trabecular meshwork with histiocytes, Touton giant cells, and eosinophils in a four-month-old white child with unilateral glaucoma who came to enucleation because of failure to control the glaucoma and suspected tumor. He states that in those cases which have come to his attention, thickening of the iris and spontaneous anterior chamber hemorrhage have usually occurred, and that once the eye

has become involved, secondary glaucoma usually develops.

Newell[6] reported two more patients with glaucoma, the first without spontaneous anterior chamber hemorrhage and the second one with. The first child, aged 10 months, had a goniotomy followed by a cyclodialysis, and finally a trephination which controlled the tension. After the cyclodialysis, the patient developed an infiltrate beneath the conjunctiva in an area where the globe had been grasped with a fixation forceps. Biopsy of this and the iris (at the time of the trephination) and of the skin lesions showed infiltration with histiocytes and giant cells. The second child, aged two and a half months, presented with a spontaneous anterior chamber hemorrhage and because the paracentesis showed "tumor cells" the eye was enucleated. The disease was confined to the anterior segment, where the iris, ciliary body, and trabeculae were infiltrated with histioctyes and Touton giant cells.

Infiltration of the iris and ciliary body has been the characteristic intraocular lesion reported. Cogan[7] reported a case of epibulbar nevoxantho-endothelioma. Both he and Maumenee cite Sanders,[8] who has collected nine cases of nevoxantho-endothelioma with intraocular involvement, all of them showing granulomatous infiltration of the iris and most presenting with spontaneous anterior chamber hemorrhage.

Fig. 1 (Kinosian). X-ray view of pathologic fracture through a cyst of the left proximal humerus.

Fig. 2 (Kinosian). X-ray view, showing periosteal reaction along the diaphysis of the femur and tibia of both legs.

The first case of intraocular involvement in generalized histiocytosis was reported by Anderson,[9] who described a case of a 16-month-old infant who presented with an osteolytic defect in the skull and an enlarged liver. The serum lipids were normal. Biopsy of the skull lesion was read as compatible with Hand-Schüller-Christian disease. Eye examination was reported to be normal, and after the child died in the acute form of the disease (Letterer-Siwe syndrome), routine section of the eye disclosed an infiltrate of histiocytes in the posterior choroid.

Case report

The following case is reported because the patient has generalized histiocytosis with unilateral secondary glaucoma as has already been described in cases of nevoxantho-endothelioma.

Fig. 3 (Kinosian). X-ray view of lytic lesion in the frontal bone.

D. B. (NYH 819557) a six-month-old Negro infant was transferred from Patterson General Hospital to The New York Hospital for further evaluation and therapy of histiocytosis. The child was born at full-term, spontaneous delivery, and was well until three months of age when his mother

Fig. 4 (Kinosian). X-ray view of lytic lesion in the parietal bone.

Fig. 5 (Kinosian). Photomicrograph of bone biopsy of left femur, showing infiltration with histiocytes.

Fig. 6 (Kinosian). X-ray view of left arm taken after admission to The New York Hospital, showing clearing of the cystic lesion and fracture through the left proximal humerus.

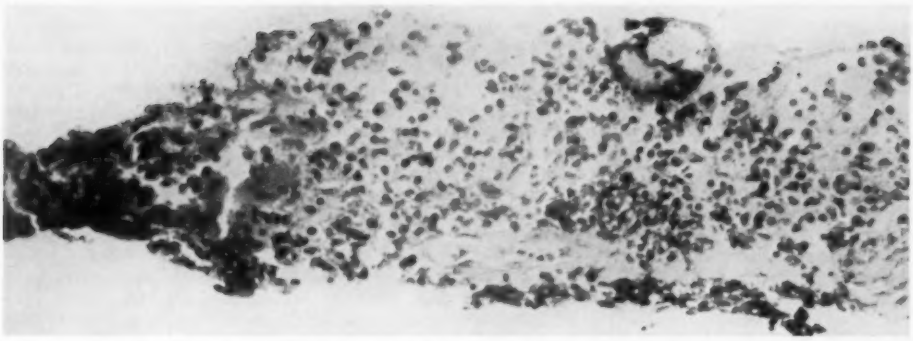

Fig. 7 (Kinosian). Photomicrograph of the iris, showing infiltration with histiocytes and Touton giant cells.

noticed that he did not move his left arm, which she then found to be swollen and tender.

X-ray films at that time revealed a pathologic fracture through a cyst of the left proximal humerus (fig. 1). Skeletal survey showed multiple areas of bone destruction with periosteal reaction along the diaphysis of the long bones and definite cortical destruction along the medial borders of the proximal metaphysis of each femur and tibia (fig. 2). Skull films showed a lytic lesion in the frontal bone and one in the parietal bone (figs. 3 and 4). The tarsal bones showed demineralization.

Physical examination revealed a mild pharyngitis; chest was clear to percussion and auscultation; heart showed a normal sinus rhythm without murmurs; and abdomen was soft with neither the liver nor the spleen enlarged.

Laboratory examinations revealed normal urinalysis, hemoglobin of 13 gm. percent, WBC 11,000 with normal differential, serum calcium of 9.4 mg. percent, phosphorus 4.4, alkaline phosphatase, 49.2 and cholesterol of 212. Bone marrow showed a predominance of lymphocytes followed by neutrophils in a ratio of 65/30 percent with five percent polychromatic normoblasts. No abnormal reticulum or fibrocytic cells were seen. Biopsy of the left femur showed histiocytosis with foam cells and giant cell formation (fig. 5).

Eye consultation noted that the child had photophobia of the right eye with an enlarged steamy cornea and bulbar conjunctival injection. A diagnosis of intracameral tumor was made. The eye was treated with pilocarpine and Neo-delta-cortef drops. The child was placed on Meticorten (20 mg.

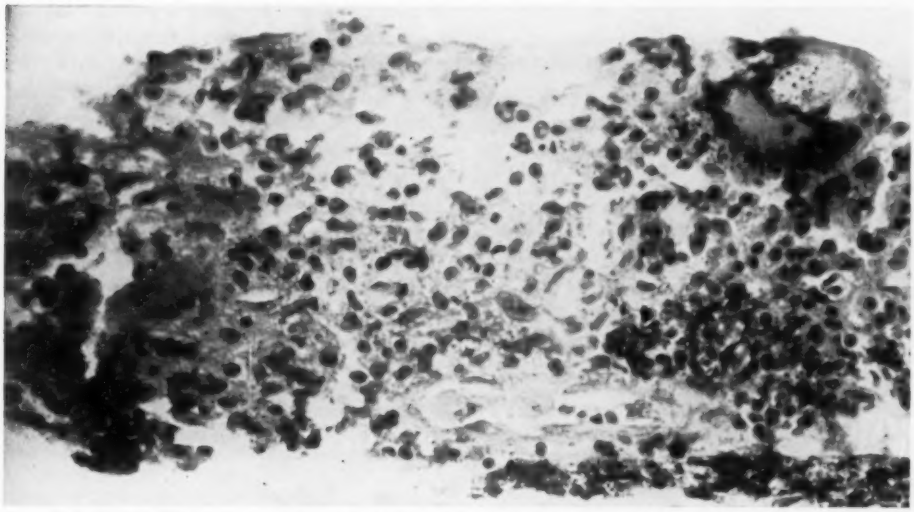

Fig. 8 (Kinosian). High-power photomicrograph of Figure 7. Sudan staining revealed the presence of both intracellular and extracellular lipoid material.

daily in divided doses) but this was without effect upon the eye. During the hospital course he developed several upper respiratory infections and a staphylococcal furunculosis of the scalp which lasted from mid-January to mid-March and finally cleared under antibiotic therapy.

Physical examination at the time of transfer to The New York Hospital revealed: temperature 37°C., pulse 100, respiration 20. The child was a well-developed, well-nourished Negro infant. Positive physical findings were limited to: skin which showed the scars of the furunculosis of the scalp and a four-cm. scar over the left thigh. The liver was palpable two cm. below the right costal margin (considered to be within normal limits).

Eye examination. Vision: the child blinked to bright objects on the right, but not on the left. The left eye was photophobic. Motility on the right was of full range but the left eye was buphthalmic and virtually filled the orbit so that motility could not be adequately evaluated. The right cornea was clear and was nine mm. in diameter; the left was scarred and steamy and the cornea was 14 mm. After clearing the cornea with anhydrous glycerine, the iris appeared to be greatly thickened and adherent to the corneal endothelium and the pupil could not be identified.

Tension as measured with the Schiøtz tonometer showed: R.E., five scale reading with a 5.5-gm. weight; L.E., three scale reading with a 10-gm. weight. Ophthalmoscopic examination of the right eye was normal.

Laboratory examination revealed a normal urinalysis. The hemoglobin varied from 11.2 to 13.5 gm. percent, WBC was 8,500 to 13,000 and showed a relative lymphocytosis, moderate anisocytosis and poikilocytosis and slight hypochromia were noted. Bone marrow showed a lymphocytosis. BUN was 7.0 mg. percent and serum cholesterol was 209 mg. percent.

A series of skeletal X-ray films taken on admission showed residual periosteal elevation in the shafts of each femur and tibia. The upper extremities were normal (fig. 6), as were the spine and pelvis. Skull films showed an area of radiolucency in the region of the right lambdoidal suture which was read as being either a vascular channel or an area of bone destruction; the previously described lytic lesions had cleared.

The child was placed on Diamox (5.0 mg./kg., every six hours) but this did not alter his intraocular pressure. On the seventh hospital day he was taken to the operating room where it was intended to do an iridectomy combined with external filtration using cautery to the lips of the sclerotomy as described by Scheie.[3] Under general anesthesia a flap of conjunctiva and Tenon's fascia was prepared beginning in the upper fornix. A scratch type of scleral incision was made one mm. posterior to the limbus and the edges were cauterized with the Hildreth cautery. Since the iris was thickened and adherent to the corneal endothelium thus obliterating the anterior chamber, the posterior chamber was entered and aqueous flowed through the incision. The iris did not prolapse, therefore, it had to be grasped with a smooth forceps and an iridectomy was done. The lens was not identified, as it was small in comparison with the buphthalmic globe. Some of the zonular fibers must have been ruptured, however, as vitreous appeared at the wound. The conjunctiva and Tenon's fascia were closed with a continuous running suture of 6-0 black silk. Postoperatively, the child developed greenish material beneath the cornea due to resorbing blood. This cleared, the anterior chamber was seen to have reformed with a central pupil; his intraocular pressure has remained normal, and he no longer has photophobia.

Histologic sections of the iris showed the stroma to be infiltrated with histiocytes containing sudanophilic material (figs. 7 and 8), as in the cases of nevoxantho-endothelioma as reported by Blank,[4] Maumenee,[5] and Newell.[6] The glaucoma which results is secondary to the massive infiltration of the iris, ciliary body, and trabeculae, which, presumably, is the mechanism in this case.

Summary

A case of systemic histiocytosis with infiltration of the iris and secondary glaucoma is presented. The ocular involvement is similar to that seen with nevoxantho-endothelioma. The latter is a benign condition, and the only systemic involvement reported has been ocular. Both of these conditions have skin xanthoma in common. The occurrence of similar intraocular involvement would tend to lend support to the view that these conditions may actually fall within the same nosologic group.

323 Washington Street.

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A STUDY OF THE ACCOMMODATION OF THE PEOPLE OF INDIA*

WITH FURTHER NOTES ON THE DEVELOPMENT OF PRESBYOPIA AT DIFFERENT AGES IN DIFFERENT PEOPLES

VICTOR C. RAMBO, M.D.
Ludhiana, Punjab
AND
S. P. SANGAL, M.Sc.
Calcutta, India

In a number of chapters on refraction in ophthalmic textbooks, and in several textbooks on refraction or ophthalmic or general physiology, Donders'[1] and/or Duane's[2-4] and, in some instances, Sheard's[5] and Jackson's, tables of amplitudes of accommodation of persons of mid-European derivation are given. The presumption is that all people on earth have the same mean accommodation amplitudes at different ages and reach the age of presbyopia at about the same mean age. This is not the case.

Following a report of the practice of representative oculists in India at the International Ophthalmic Congress in London, 1950,[6] showing that there is an earlier onset of presbyopia in India, notes were published on the varying ages at which different peoples develop presbyopia.[7] It would appear that the Egyptian, the Greek, the Italian, and the people closer to the equator develop presbyopia earlier, and Scandinavian peoples later, than mid-European peoples.

Stenius[8] writes: "According to my investigations (1) the average age when persons with 'presbyopic troubles' come to the ophthalmologist for help with their near work (reading) is (independently of refraction) 45.4 years. (2) Emmetropes need help at 48 years. (3) The average need of a total correction for near when persons come to the ophthalmologist is $+1.00 \pm 0.06$ dptr. (4) The average need of $+1.00$ dptr. addition for near sets in at about 48 years."

Considering the problem, it appeared that near the tropics, also, there is never as much accommodation from birth to presbyopic age, or having the same accommodation (or perhaps even more) at birth, the accommodation decreases at a more rapid rate. One of us (V. C. R.) determined to make sufficient accommodation studies of Indian people so that tables of accommodation at different ages could be prepared. This has been done and the results are here presented according to Donders and Duane, called in this paper "Duane," with modifications hereunder described. Also sufficient material was collected from persons up to the age of 37.5 years of age to permit presentation of statistics of accommodation obtained by Sheard's method.

* From the Department of Ophthalmology, Christian Medical Colleges at Vellore and Ludhiana, and the Christian Hospital, Mungeli, India, and the Psychometric Research and Service Unit of the Indian Statistical Institute, Calcutta. Mr. S. P. Sangal prepared the statistical analyses and graphs from the clinical data.

The literature gives no details of the origin of the persons who were examined by Donders and Duane. Knowing the time and place of the studies, however, it was concluded that the persons examined were probably of mid-European origin. Sheard in a personal communication affirmed that his statistics were obtained from persons whose origins were in middle Europe. Guidance in this six-year investigation was given by Edwin F. Tait,[9] M.D., of Temple University, Philadelphia. He asked me to stress that in such an investigation no objective method is possible. All observations are subjective and influenced by conditions which include the state at the moment of both the investigator and of the investigated, and the quality of the surroundings, which can never be exactly the same again. The same investigator, testing the same person at another time and circumstance, would arrive at a figure which may or may not be the same as that previously obtained. However, though the figures taken by somewhat different methods are studied side by side, the comparisons do bring out indisputable facts that are worthy of acceptance and of application in clinical practice. Dr. Tait called attention to the fact that Duane measured accommodations for his study, not from the eye itself, but from its anterior focus (14 mm. in front of the cornea); while the measurements herein presented* were taken, as recommended by Tait, from the limbus. Duane's study would give, particularly in the younger ages, accommodation figures that would be higher.

It is to encourage further research that more details have been given in this paper than would ordinarily be necessary just for the presentation of the findings. This presentation should stimulate the study of accommodations of other groups.

The relative accommodative amplitudes are presented up to the age of 60 years. Approximately 100 eyes were examined in each group from 10 years up to and including the age of 37.5. After this, the numbers of observations from which the statistics are drawn are less as the variations were less marked in the higher age groups.

Age groups were chosen as given in Donders' and Duane's determinations, that is, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60 years of age, with this difference: As the numbers of those whose accommodation was determined increased, it became clear that the change which took place in the accommodation from age group to age group was too great, and that supplementary intermediary age groups should be added. This was done by adding the group of 27.5, 32.5, 37.5, 42.5, and 47.5.

The convention was accepted that accommodation findings for the eyes of any person would be used if his age was within six months of the age set for any group. The age of "30" years means that the person was aged between 29.5 and 30.5 years. The age of "37.5" means that the person was between 37 and 38 years, and so on. All others were rejected. There being little change in the mean of the accommodation amplitude after 42.5 years, a slightly wider range of time was allowed for each age group above this.

It was decided to have a cross section of the people of the cities and of the villages. While dealing with students and their teachers and other educated people, the age records and the personal statements were our assurance of accuracy in this respect. In the villages, however, many knew their ages only approximately. At times there would be 15 or 20 people around the investigator,

* Fincham,[10] of the Institute of Ophthalmology, London, Cooper,[11] Editor of the *Journal of All India Ophthalmological Society*, Bombay, and others, gave advice. Always the advice was carefully considered. Final decision had to be made by me and the responsibility for the decisions is mine only. Dr. C. Deen, in Mungeli, and Dr. Roy Ebenezer, in Vellore, helped to make the research possible by shouldering extra duty in their clinics while I was out getting the statistics. I am grateful to all these associates in the work. The friendliness, good humor, and co-operation of many hundreds of people in bazaars, court houses, schools, village and town roads have made the collection of data a pleasant and enriching experience. (V. C. R.)

none of whom knew their ages accurately. Some would say—"I was born the year of the flood in the local river" or "the year that Ghandji visited my village."

Though some misrepresented their ages in an attempt to get their test made along with others, each individual was evaluated as correctly as possible in order to be satisfied that the person was within the group into which the notation of the amount of his accommodation was to be placed. Hundreds who were doubtful about their ages, or about whose ages there was any doubt, were excluded.

At the beginning of the study, it was thought that the accommodation of both males and females might be taken for these statistics. This was not possible, but sufficient females at the presbyopic age were tested to suggest that the difference in accommodation between males and females might compare with the statement of Charamis[6] that, in Greece, women develop presbyopia one year before men. It may be that the arms of women are sufficiently shorter than their male counterparts to cause them to come for a reading addition sooner than men come for theirs. It need not necessarily mean that they have any difference in their accommodations.

In every person tested, distance vision of each eye was taken separately, found to be 6/6 or 6/5 nearly always without correction, but a few had vision corrected to this acuity with glasses. Some refractions were done on the spot. In nearly all of those under the age of 40 years +1.25D. sph. was added and found to blur the distance vision. This presumably ruled out some persons with definite hypermetropia.

All the tests here reported were on Indians residing in India; no person of other countries or of mixed East and West descent was included. All appeared well except for one man who had been ill with fever and was convalescent but whose accommodation was well within the average of others who were well and strong. All walks of life are represented—students, teachers, blacksmiths, mechanics, farmers, officials, police, laborers, doctors, nurses, the retired, just anybody as they came along and for whom their ages could be established for inclusion in our statistics.

Their origins were from the north and from the south, from the east and from the west, but most were residents of the Vellore and Mungeli areas.

It is probable that if separate graphs were prepared for different sections of a subcontinent such as India, they would show minor differences.

Certain adjustments had to be made in the instructions given by Dr. Tait. For instance, Dr. Tait sent cards with the letters EFT printed on them for use in determining the near-point. It was found that the use of letters in either English, or Hindi, or Tamil, or Telegu distracted from the purpose of our investigation. For convenience and uniformity "+" mark was adopted, each line of which was approximately 4.0-mm. long and 0.25-mm. wide. This mark was made with a pen with black or blue ink on white paper. It gives satisfactory fixation, is available anywhere and is hereafter referred to as "the object."

At first we tried to get the near-point by the standard Duane method, gradually bringing the object closer and closer to the eye until it reached the position where the fixation object did not stand out so clearly. The distance of the object from the patient's limbus was then measured as accurately as possible and calculated in diopters. This was called the "clear-to-blur" method.

It was soon found that the patient often had so much difficulty in the determination of what Tait calls "Duane's near-point blur" that the patient, and the doctor, were led into uncertainty. To explain to an illiterate person, who was straining every faculty to cooperate with the examination, just at what place the object "does not stand out so clearly" not only took a long time but there was, too frequently, doubt in the determina-

TABLE 1

MALES AGED 10 YEARS

No.	Name	c+1.25 addition Duane (V.C.R.) O.D.	O.S.	Duane O.D.	O.S.	(V.C.R.) O.D.	O.S.	Sheard O.D.	O.S.
1	Rathakrishnan*	6/6	6/9	6/12	6/12	11	—	13	—
2	Punniakotti	6/6	6/6	6/18	6/12	14	14	12.5	—
. . . . .									
50	Kamalakama	6/6	6/6	6/18	6/18	11	14	12	10
51	V. Subramanian	6/6	6/6	6/6	6/6	12.5	12.5	10	10

Vision of the left eye was 6/9 and was therefore, excluded from the record; only the right eye accommodation was included.

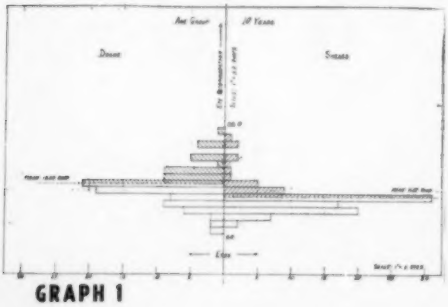
tion. Since Costenbader[12] reported that the "out-to-clear" method gave more "consistent" and accurate results, and Sheard[5] did not follow Duane's example in accepting the first impression of "blur" as the measuring point but established the "clear" or distinct impression from which he would measure the accommodation by his method, the following, which in this paper will be called the "blur to clear" method, was adopted and found satisfactory.

The procedure was explained to each patient and repeated to make sure he understood what he was to do. The patient selected wore his correction for distance, if necessary, and with one eye occluded by an obturator in a trial frame, moved the object along a half-meter measuring stick so close to the unoccluded eye that there was a complete blur of the object. The object was then moved out slowly until the patient saw it clearly. The distance of the object from the patient's limbus was then measured and calculated in diopters. The process was then repeated for the second eye.

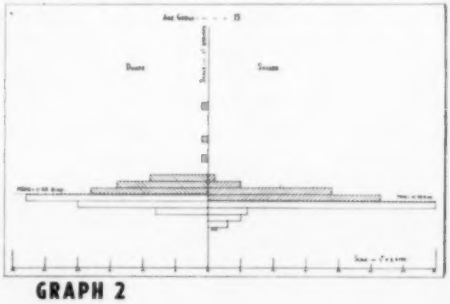
The clear-to-blur method was not changed to blur-to-clear without investigating the comparative statistical consequences. Therefore, 114 determinations of accommodation were taken on educated men of different ages who showed unhampered ability for fine observation and willingness to undergo the tests. Fifty-seven of the determinations were taken on the same eyes with the blur-to-clear method.

The average of accommodation taken by coming from clear-to-blur was only 0.129 diopter (approximately one-eighth diopter) more than the average of determinations taken by blur-to-clear method. We took this analysis as sufficient evidence that there is no significant difference between these two methods. The total accuracy of the findings can be depended upon because of the greater accuracy with which the average patient comprehended the position of the "clear" object in the blur-to-clear method.

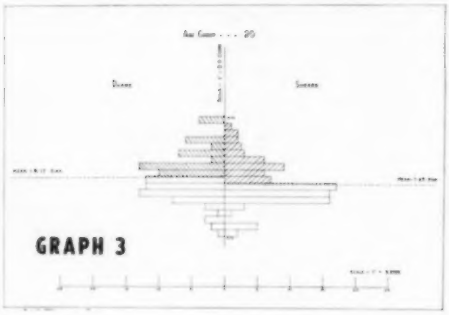
To determine the accommodation of presbyopics a +3.0D. lens was added to the unoccluded eye and the measure of the near-

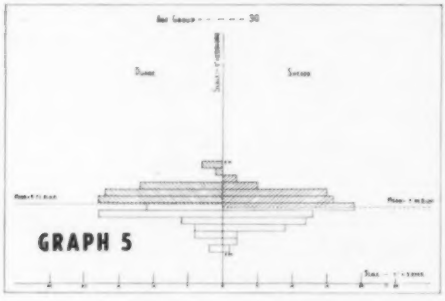


GRAPH 1



GRAPH 2





point was taken in diopters and the 3.0D. was deducted from the total, leaving the accommodation exerted by the presbyope.

A sample of the form for taking entries of accommodations with the first and last two entries at 10 years is given in Table 1.

Different individuals and even the two eyes of the same individual may respond with different decreases in vision on the addition of the +1.25D. lens.

We note in the record of Case 51 (table 1) that the subject did not lose visual acuity with the addition of the convex lens. He should have been refracted and then had his accommodation taken or been excluded from the record.

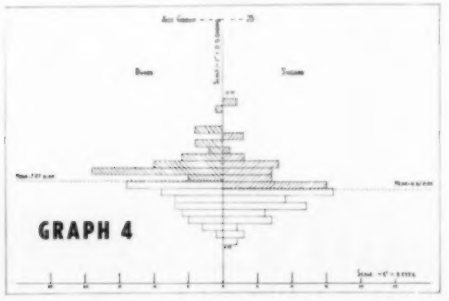
The determination of the accommodation by the method of Sheard[9] involved the following procedure:

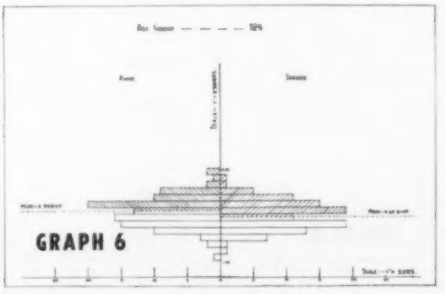
The patient fixed monocularly upon the object, which is set up at one-third meter from the limbus. If the patient is nonpresbyopic or early presbyopic, he will see the object clearly. Concave spherical lenses are then introduced, increasing in −0.5D. steps until the patient reports that the object has blurred and he can no longer see it clearly. The concave lens value is now decreased until the object is seen clearly. This concave value added to the 3.0D. which were necessary to fix the object in the first place at one-third meter represents the accommodation. For example, if a patient was able to see the object clearly with a −2.0D. lens (but could not see it clearly with a −2.5D. lens), his accommodation would be the 2.0D. he used to overcome the concave lens power, added to the 3.0D. used to fix the object at 33 cm. in the beginning, that is 5.0D.

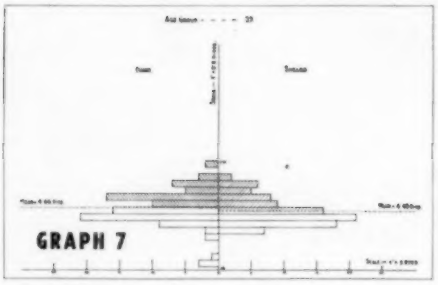
Testing of accommodation of presbyopics could also have been done with Sheard's method but it was not felt that it was necessary, so Sheard's statistics have been omitted for the less than three-diopter presbyopes.

Nature of the Data

The measurements of the accommodation for the different age groups were taken by two methods, Duane's and Sheard's.





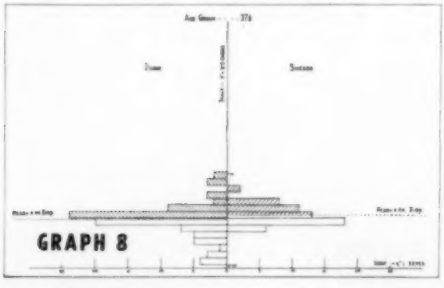


GRAPH 7

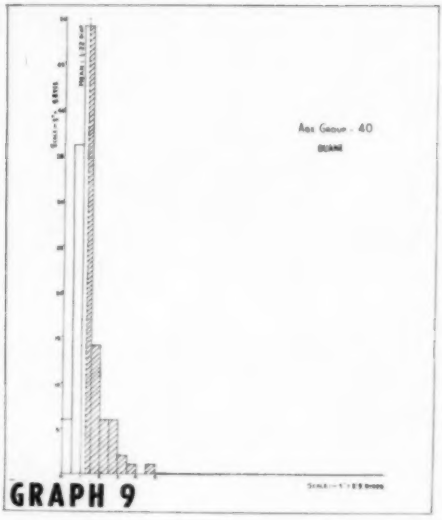
The data were first scrutinized for any inconsistencies or omissions. Histograms were prepared for each age group separately, both for Duane's and Sheard's for the Indian statistics. Up to 37.5 years of age, these have a common base, Graphs 1 to 8. Above 37.5 years of age Sheard's statistics were not available so Graphs 9 to 13 include only Duane's. This study was done to get an idea of the nature of the distribution and to summarize the tables.

In age group 10 years, the interval was taken as one diopter because the range of accommodation was very large. In all other cases, the interval was taken as 0.5 diopter. It was assumed that the value from all the eyes falling in a particular class were the values of the midpoint in that class.

The distributions from age group 42.5 years and over (graphs 10-13) show that the number of persons with higher accommodations decreases very rapidly and that the majority is concentrated in the lower-accommodation group.



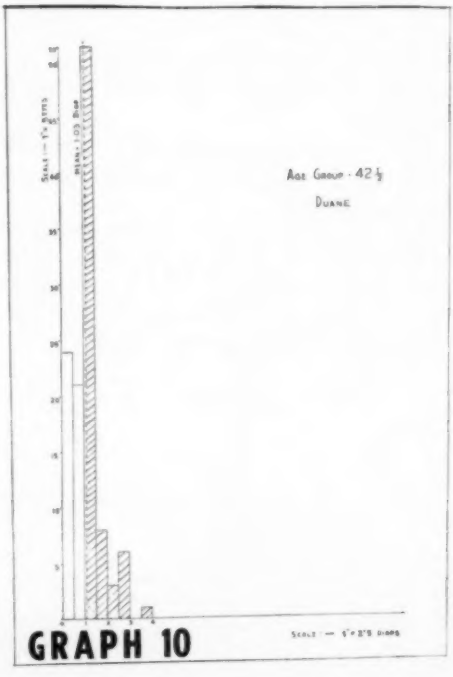
GRAPH 8



GRAPH 9

LEFT VS. RIGHT EYE

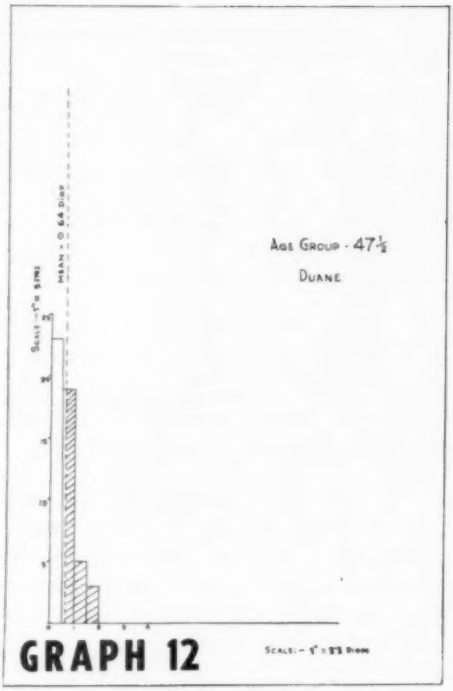
It is known that, if the accommodation of the left eye and of the right eye is measured



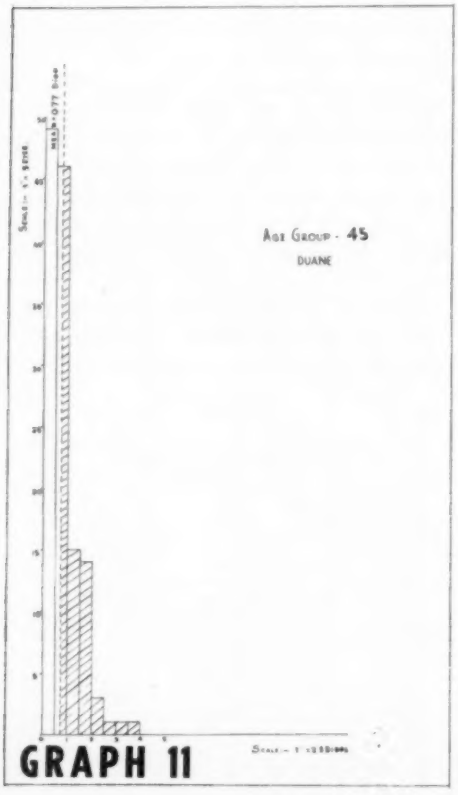
GRAPH 10

separately, small differences will be observed. Before an estimate of the average accommodation for both eyes can be used, it should be determined whether the observed differences between eyes are real differences or occur simply because of chance factors. Tables 2-A and 2-B show the "t"[14] values and "sign test"[13] data, respectively, for the Duane method.

To substantiate further the conclusion that there is no real difference between left and right eye accommodation, another test was used. From Tables 2-A and 2-B we see that there are four significant values out of 14 groups. It may now be asked: "Are these four significant values due to chance?" "How many significant values can result just by the operation of chance factors?"



GRAPH 12



GRAPH 11

GRAPH 13

TABLE 2A

"t" VALUES FOR THE DIFFERENCES BETWEEN THE LEFT AND RIGHT EYE FOR DUANE

Age Group	Degrees of Freedom (n−1)	L-R Eye Mean Difference	S.D.	"t"	Probability
(1)	(2)	(3)	(4)	(5)	(6)
10.0	49	0.722	1.946	−2.597*	0.0128
15.0	49	−0.222	0.834	1.850	0.0833
20.0	49	−0.286	0.713	2.807†	0.0069
25.0	49	0.026	0.713	0.255	0.9485
27.5	45	−0.120	0.668	1.205	0.2444
30.0	45	−0.021	0.415	0.347	0.8511
32.5	49	−0.131	0.504	1.831	0.0833
35.0	44	−0.085	0.266	2.061*	0.0428
37.5	41	0.030	0.457	0.421*	0.8094
40.0	55	−0.068	0.243	2.073*	0.0468

* Indicates significant difference at the five-percent level. If we find a significant value of "t," we conclude that there is a difference between the two means. If it is not significant, we accept the hypothesis that there is no difference.

† Significant difference at the one-percent level.

This question is answered by the "P"[15] test, in which the actual probabilities of getting the "t" values equal to or greater than the observed values for each age group are combined into a single statistic by the following transformation:

$$X^2_{2k} = -2\sum_{i=1}^{k} \log_e P_{\lambda i}$$

Where $P_{\lambda i}$ = the probability of getting the "t" value greater than or equal to the observed value for the i_{th} age group, K = number of age groups and $P_{\lambda i}$ is obtained from column 6 in Table 2-A and column 5 in Table 2-B. We find that $X^2_{28} = 11.213$ which is not significant at the one-percent level. Thus it can be concluded that these significant values have occurred by chance alone and there is no real difference between the left and the right eye.

This procedure was repeated for the Sheard method, and Table 3 shows the results at various age levels. A significant difference can be observed for age 27.5 years, but once again the P_λ test yields the value of $X^2_{16} = 6.149$, which is not significant at the one-percent level, and the same conclusion can be drawn for Sheard's as was drawn for Duane's data, namely, that there is no real difference between the accommodations of the left eyes and right eyes.

TABLE 2B

SIGN TEST FOR THE DIFFERENCE BETWEEN LEFT AND RIGHT EYE*

Age Group	(+ve)	(−ve)	0	Probability
42.5	16	21	18	0.2950
45.0	20	22	16	0.4478
47.5	4	12	7	0.0723
50.0	11	22	15	0.0658

* For most of the age groups, no real difference appears to exist between the accommodation of the left and right eye. In age group 20, however, there is a significant difference between the left and the right eye. Age group 10 and 35 also throw some doubt on the equality of accommodation for the left and the right eyes for Duane's. One explanation for age group 10 may be that children are not keen observers.

TABLE 3

"T" VALUES FOR THE DIFFERENCE BETWEEN LEFT AND RIGHT EYE FOR SHEARD

Age Group	Degree of Freedom	(L-R)	S.D.	(L-R) eye
(1)	(2)	(3)	(4)	(5)
10.0	49	−0.215	1.181	1.274
15.0	49	0.090	0.676	0.932
20.0	49	−0.087	0.630	0.967
25.0	49	−0.166	0.523	2.219*
27.5	45	−0.141	0.332	2.852†
30.0	45	0.005	0.480	0.076
32.5	49	−0.079	0.400	1.391
35.0	42	−0.069	0.378	1.188
37.5	26	−0.071	0.426	0.850

* and † See Table 2A.

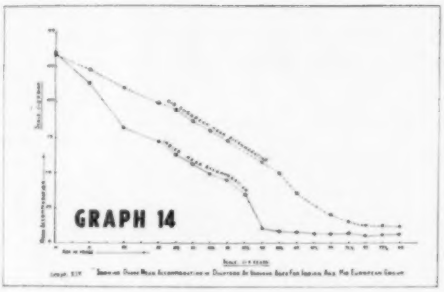
Since we have now concluded that there is no difference between the left and the right eye accommodations, a table of mean accommodation can be established for the Indian group in order to compare it with the mid-European group. This was done only for the Duane method.

Since the mean is calculated from a sample only, it is subject to sampling errors. We can, however, estimate statistically from the result of a single sample a range within which we can be 99-percent confident that the true mean will lie. The means and their confidence limits are shown in Table 4 for each age group.

Mid-European accommodation

The table for mean accommodation for the Indian group can now be compared with the mid-European group. The near accommodation for both the groups is plotted in Graph 14.[16]

The first striking feature of the graph is that the mean accommodation for the Indian group is always, except for the 10-year



group, lower than the mid-European group. (The difference for age group 10 years is almost negligible.) It may be that all people start with the same accommodation initially.

The second important feature of the graph is that the accommodation of the Indian group falls more rapidly than the counterpart in the European group. This shows the earlier onset of presbyopia in the Indian group.

TABLE 4

Mean accommodation for each age group and 99 percent confidence interval for the mean, Duane method

Age	Standard Error	Lower Limit	Mean	Upper Limit
(1)	(2)	(3)	(4)	(5)
10.0	0.368	12.54	13.52	14.51
15.0	0.208	10.76	11.32	11.87
20.0	0.253	7.55	8.23	8.91
25.0	0.245	6.60	7.26	7.92
27.5	0.214	5.72	6.29	6.87
30.0	0.162	5.25	5.69	6.12
32.5	0.162	4.50	4.94	5.37
35.0	0.210	4.08	4.65	5.21
37.5	0.205	3.00	3.55	4.10
40.0	0.083	1.01	1.22	1.42
42.5	0.087	0.83	1.03	1.24
45.0	0.064	0.60	0.77	0.95
47.5	0.067	0.42	0.64	0.87
50.0	0.040	0.50	0.62	0.74

The values given under "upper" and "lower" columns are not to be treated as if they are the highest or the lowest observable values of the accommodation at a particular age. It is possible that the true mean lies outside these limits, but it is highly improbable.

TABLE 5

Mean accommodation for mid-European and Indian groups

Age	Mean Accommodation		Difference between Mid-European —Indian Accommodations
	Mid-European	Indian	
(1)	(2)	(3)	(4)
10.0	13.4	13.52	−0.12
15.0	12.3	11.32	0.98
20.0	11.1	8.23	2.87
25.0	9.9	7.26	2.64
27.5	9.5	6.29	3.21
30.0	8.7	5.69	3.01
32.5	8.1	4.94	3.16
35.0	7.3	4.65	2.65
37.5	—	3.55	—
40.0	5.8	1.22	4.63
42.5	5.0	1.03	3.98
45.0	3.6	0.77	2.91
47.5	—	0.64	—
50.0	1.9	0.62	1.37
52.5	1.6	0.78	0.82
55.0	1.3	0.59	0.71
57.5	1.3	0.68	0.62
60.0	1.2	0.68	0.52

Note: Dashes indicate that these values are not available. The figures for age group 55 and 60 are not reliable due to the lack of sufficient observations. It was much more difficult to find persons with 6/6 vision in 55 and 60 year age groups than in the lesser age groups. However, examination of the graph suggests that the figures will not change appreciably.

TABLE 6

SHOWING THE PERCENTAGE OF EYES HAVING ACCOMMODATIONS ABOVE AND BELOW THE MEAN

Age Groups	Number of Eyes	Duane		Sheard	
		% above the mean	% below the mean	% above the mean	% below the mean
10.0	100	39.9	60.1	31.9	68.1
15.0	100	40.8	59.2	48.9	51.1
20.0	100	46.4	53.6	45.9	54.1
25.0	100	49.0	51.0	47.6	52.4
27.5	92	49.2	50.8	49.1	50.9
30.0	92	50.7	49.3	53.9	47.1
32.5	100	51.0	49.0	48.2	51.8
35.0	90	50.4	49.6	43.8	56.2
37.5	84	55.7	44.3	43.8	56.2
40.0	112	47.9	52.1		
42.5	110	59.6	40.4		
45.0	118	43.2	56.8		
47.5	46	44.4	56.6		
50.0	96	42.9	57.1		

The marked feature is that there are two sharp falls in the graph for the Indian group: (1) 11.3D. to 8.2D. from 15 years to 20 years of age; (2) 3.5D. to 1.2D. from 37.5 years to 40 years of age.

This seemingly more rapid fall of accommodation at the beginning of the presbyopic age is not as acute as the graph seems to show. On or about the entrance into the presbyopic stage both the method for presbyopics and the method for nonpresbyopics can be used for determining the relative amplitude of accommodation. If the accommodation of a person is measured by both of these methods it is always found that the method used for presbyopes (addition of a plus-three lens and then the deduction of these three diopters in calculating the accommodation) always gives a somewhat lesser figure. As decreasing accommodation demands the change of method so that soon all accommodations must be taken by the method for presbyopics; results using this method, giving a lesser figure, will show an initial rapid fall. And it may be that it gives a less than actual measure of accommodation in the graphs. One wonders how the graph for mid-Europeans (Duane) could have been made with so little of this more rapid fall as the patients went into the presbyopic age, when less than 3.0D. of accommodation had to be measured.

From age group 45 years and over, the Indian line is almost horizontal. From age group 55 years the mid-European line is also almost horizontal. This shows that the ac-

TABLE 7

PERCENTAGE OF EYES WITH ACCOMMODATION THREE DIOPTERS AND BELOW

Age	Duane	Sheard
Below 30	0.00	0.00
30.0	3.12	2.08
32.5	2.88	1.92
35.0	6.12	7.61
37.5	22.73	10.34
40.0	96.19	—
42.5	99.00	—
45 and above	100%	—

Note: Dashes indicate unavailability of data.

TABLE 8

"t" VALUES OF THE DIFFERENCE BETWEEN SHEARD AND DUANE MEAN ACCOMMODATION

Age Group	Degrees of Freedom	Mean	S.D.	"t"
(1)	(2)	(3)	(4)	(5)
10.0	49	3.711	6.796	3.822†
15.0	49	1.722	0.860	13.878†
25.0	49	1.365	2.953	3.235†
27.5	45	1.490	2.624	2.8098†
30.0	45	0.793	1.846	2.882†
32.5	49	0.663	1.917	2.421*
35.0	42	0.863	1.687	3.316†
37.5	26	0.584	1.268	2.349

* and † See Table 2A.

commodation remains almost constant after a certain minimum is reached.

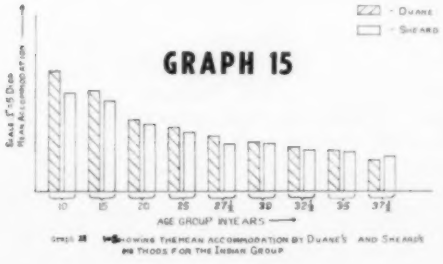
This minimum is practically the same in both groups and clinically can be considered the same. It is generally agreed that when a person has an accommodative amplitude of only 4.0D. he enters the presbyopic age, and when he has an accommodation of only 3.0D., he is definitely in the presbyopic age. Taking the latter as the criterion, it is seen from the graph that the presbyopic age for the Indian group starts at about 38 years, while it starts at a little over 46 years in the mid-European group.

Table 5 shows the magnitude of difference between mid-European and Indian mean accommodation. The maximum difference is at the age of 40 years. As the groups advance in age, the difference narrows down. This indicates that accommodation in the older age groups attains a minimum which varies little from country to country.

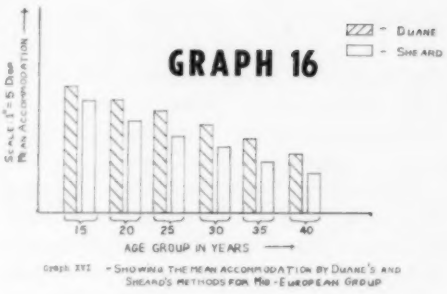
Interpretation of Average Accommodation

Graphs 1 to 8 show accommodations taken by Duane's and Sheard's methods for each age group. A central dotted line coincides with the mean of the distribution. The shaded portion gives the number of people that have accommodations above the mean.

From Graph 8 and Table 6 it is seen that for age group 37.5, which is almost the mean presbyopic age (this being 38 years) 44 percent of eyes are entering presbyopia, whereas 56 percent are not. Thus the presbyopic age does not mean that a person falling in that age group needs correction for presbyopia, and vice versa.



Graph XV - Showing the mean accommodation by Duane's and Sheard's methods for the Indian Group



Graph XVI - Showing the mean accommodation by Duane's and Sheard's methods for Mid-European Group

The foregoing inference is further supported by Table 7 which gives the percentage of eyes having accommodation of 3.0D. or less for each age group. From this table we see that there are eyes which may need correction for presbyopia as early as 30 years of age. Another important feature that emerges from this table is the big increase in presbyopia between the ages of 35 and 40 years.

It thus becomes clear that an individual is to be treated as an individual and his needs are his own specific needs, and the individual is not to be given correction for presbyopia merely because he is in the presbyopic age of his country, and vice versa.

Duane vs. Sheard

Since both Duane's and Sheard's methods were used in measuring accommodation, it may be asked: "Do the two methods measure the same thing?" or "Are the observed differences between the two methods consistent with the hypothesis that both methods measure the same thing?" This, again, can be answered by the "t" test technique. Table 8 gives the "t" values for the difference between Sheard's and Duane's mean accommodations. For every age group the difference is significant at the 0.05 level. The only valid conclusion, therefore, is that the two methods measure different things relating to accommodation.

Since the observations for both the Duane and Sheard determinations were made on the same individuals, and if the methods measure the same things, then the average accom-

modation should be the same. However, from Table 8 it is clear that this is not true. The stimulation for accommodation in the different methods is different and the responses are different, the Sheard in each instance being less than the Duane.

Amplitude of accommodation is not a fixed value but is relative to the method used to determine it. Five different methods will give five different results in the same individual (in the prepresbyopic and early presbyopic ages). Moreover, Graph 15 demonstrates that in all cases, except those in age group 37.5 years, the mean Duane accommodation is higher than the Sheard for the Indian group. Graph 16 shows this also true for the mid-European group except that the mean is higher for all ages.

Conclusion

Method and statistics of an accommodation survey and an average accommodation table for East Indian males are presented.

The accommodation of Indians, practically the same as for mid-Europeans at the age of 10 years, falls more rapidly, and the presbyopic age is reached about eight years sooner than mid-European graphs indicate. Donders', Duane's, or Sheard's statistics and graphs of accommodations are not valid for Indians and probably are not valid for large portions of the human race.

All peoples do not have the same average accommodation at given ages. No longer should one speak of the "presbyopic age"; rather, "presbyopic ages."

After the early thirties, every refraction patient should have accommodation taken. Special attention might be given to migrants from other countries, but whether migrant or not each individual should have accommodation taken as the presbyopic ages are approached or entered. After a native of India reaches the age of 45 years this is not so important and full addition for close work or reading can usually be given. The two methods of measuring accommodation (Duane's and Sheard's) give different results. These methods should be further investigated to find which one is the more correct. At present it is sufficient to take the accommodation by the blur-to-clear method described in this paper, using the universally available inked cross or plus mark as the object of fixation.

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RETINAL HEMORRHAGES IN THE NEWBORN*

CONRAD L. GILES, M.D.
Ann Arbor, Michigan

The appearance of hemorrhages in the retina of the newborn infant has been a well-documented observation for over 100 years. Authorities still speculate, however, as to the exact etiology and incidence of these hemorrhages.

The purpose of this paper is to present the ophthalmoscopic findings in a series of 100 newborn infants all of whom were examined within one hour after birth. Careful analysis of these cases has suggested that a factor heretofore unmentioned—the sudden release of intracranial pressure—may actually play an extremely important etiologic role.

HISTORICAL BACKGROUND

Jaeger,[1] in 1861, is generally credited as the first clinician to report retinal hemorrhages in the newborn. Many authors since have studied the fundi of newborn infants in an attempt to determine the incidence, etiology, and significance of the hemorrhages.

The figures given for the incidence of these hemorrhages range from 2.6 percent[2] to 59 percent.[9] Koenigstein,[4] in 1884 found 29 cases of retinal hemorrhages in a series of 281 newborns (10 percent), Howland[5] three percent of 400 in 1926, Edgerton[6] 41 percent of 458 in 1933, Falls and Jurow[7] 32.6 percent of 432 in 1946, Chace[2] 2.6 percent of 839 in 1950 and in the most recently reported series M. Luther Kauffman[8] found hemorrhages in 18.2 percent of 7,727 infants examined.

The variety of percentages given for the incidence of retinal hemorrhages is rivaled only by the number of theories suggested to explain their presence.

Koenigstein[4] felt that the hemorrhages occurred during the first act of respiration and that pressure exerted on the infant at birth was not a factor in their production. Schleich[9] stated that increased pressure within the cavernous sinus with subsequent congestion of the ophthalmic veins and increased venous pressure coupled with the fragility of the newborns' blood vessels caused the hemorrhages. Paul[10] was of the opinion that the congestion was secondary to loops of cord around the neck, and that this was the factor responsible for the hemorrhages. Subsequent investigations by others[3, 11, 12] did not confirm this impression. Wolff[11] implicated asphyxia while Ehrenfest[12] felt that a hemorrhagic diathesis was present in those infants manifesting retinal hemorrhages at birth.

Most of the recent investigators[6, 7, 13, 14] suggest that the hemorrhages are a result of obstetric trauma and the not uncomplicated passage of the infant through the birth canal, but fail to pinpoint a definite mechanism for their production.

The significance of retinal hemorrhages remains indefinite. Early writers[9, 15–17] on the subject felt that these hemorrhages were often associated with intracerebral damage and therefore were alarmed at their presence. It is now, however, generally agreed that the hemorrhages probably have little relationship to either cerebral damage or later ophthalmologic disease.[8, 18, 19, 20]

METHOD OF STUDY

This report deals with a series of 100 full-term newborn infants delivered in Beyer Memorial Hospital (Ypsilanti, Michigan) between March 8 and April 29, 1958. I was present at each delivery as either first assistant or attending physician.

Each infant was examined ophthalmoscopically, as well as externally, within one hour

* From the Department of Ophthalmology, The University of Michigan Medical School. Read in part before the residents' meeting of the Detroit Ophthalmological Society, January 29, 1960.

TABLE 1

RELATIONSHIP OF HEMORRHAGES IN THE NEWBORN TO PARITY OF THE MOTHER

Number of primipara infants	22
Number of multipara infants	78
Percentage of retinal hemorrhages in primipara infants	45%
Percentage of retinal hemorrhages in multipara infants	38%

after birth using the technique described in an earlier report.[21] Briefly presented this method of examination involved instillation of solutions of one-percent Cyclogel and 10-percent neosynephrine 15 minutes apart, mummification of the child and restraint of the infant's head by a nurses' aide.

All of the infants were examined at approximately 24-hour intervals. Those infants with positive funduscopic findings were followed until the disappearance of the retinal hemorrhages (or until the time of discharge) and those with negative findings were followed for 48 hours.

The parity of the mothers, premedications used, duration of labor, anesthetics employed, method and control of delivery, weight of infant, and degree of cyanosis and the findings of the ophthalmologic examination were all carefully recorded.

DATA

1. INCIDENCE OF RETINAL HEMORRHAGES

Of the 100 infants examined 40 percent exhibited retinal hemorrhages. Most of these hemorrhages were located in the disc-macula area and could be placed in three categories.

The most frequently seen type of retinal hemorrhage was flame-shaped and located above and below the optic disc. These varied in number from one or two small areas to massive retinal hemorrhages but usually were resorbed quite quickly, often within 24 to 48 hours after their appearance.

A less common finding were grossly round hemorrhages, seen near the disc, usually larger than the flame-shaped hemorrhages, being one to two disc diameters in size and fewer in number. This type of retinal hemorrhage remained the longest, some being seen seven to 10 days following birth.

The rarest of the three types was a thin sheetlike hemorrhage extending radially from the disc to the periphery. This type tended to disappear in three to six days.

2. INFLUENCE OF PARITY

There were 22 primipara and 78 multipara mothers in the series (table 1). Ten of the babies born to primipara mothers, representing 45 percent of the group, manifested retinal hemorrhages while 30 of the 78 children born to multipara mothers or 38 percent exhibited the hemorrhages.

3. FORCEPS VS. SPONTANEOUS DELIVERY

Fifty-three percent of the cases were delivered with the aid of forceps. In most cases outlet or low forceps were used but midforceps were used in one case, multiple forceps

TABLE 2

RELATIONSHIP OF METHOD OF DELIVERY TO HEMORRHAGES

A. SPONTANEOUS DELIVERIES	
Number and percentage of spontaneous deliveries	47
Number of infants with hemorrhages	16
Percentage of infants with hemorrhages	34%
B. FORCEPS DELIVERIES	
Number and percentage of forcep deliveries	53
Number of infants with hemorrhages	24
Percentage of infants with hemorrhages	45%

TABLE 3

METHOD OF DELIVERY AS RELATED TO PARITY AND THE APPEARANCE OF RETINAL HEMORRHAGES

A. PRIMAPARA MOTHERS	
Number delivered spontaneously	10
Number in this group with retinal hemorrhages	9
Percentage of hemorrhages in this group	90%
Number delivered with forceps	12
Number in this group with retinal hemorrhages	1
Percentage of hemorrhages in this group	8%
B. MULTIPARA MOTHERS	
Number delivered spontaneously	37
Number in this group with retinal hemorrhages	7
Percentage of hemorrhages in this group	29%
Number delivered with forceps	41
Number in this group with retinal hemorrhages	23
Percentage of hemorrhages in this group	57%

applications in eight cases and oblique application of the forceps occurred in two cases. Twenty-four out of the 53 cases or 45 percent demonstrated retinal hemorrhages.

In the group of infants delivered spontaneously 16 (of 47) or 34 percent exhibited the hemorrhages (table 2).

Ninety percent of the 10 infants of primapara who were delivered spontaneously exhibited hemorrhages, while retinal hemorrhages were seen in only one out of the 12 (eight percent) of the infants in the primipara group in whom forceps were used (table 3).

The reverse of the above situation was noted in the multiparous group where application of forceps resulted in a higher percentage of hemorrhages (23 out of 41 or 56 percent) than in the group delivered spontaneously (seven out of 37 cases or 29 percent).

4. WEIGHT OF INFANT AND METHOD OF DELIVERY

Table 4 lists the average and median weights in the groups with and without hemorrhages and those delivered with and without forceps. The differences are insignificant and need not be further commented upon.

5. DURATION OF LABOR

The mean duration of the first and second stages of labor (that is, from the onset of rhythmic uterine contractions until the delivery of the child) in those infants delivered by means of low forceps and exhibiting no retinal hemorrhages was seven hours and 15 minutes and in those presenting retinal hem-

TABLE 4

WEIGHT OF INFANT, METHOD OF DELIVERY AND PRESENCE OF HEMORRHAGES

A. SPONTANEOUS DELIVERIES	
Number of infants *without* retinal hemorrhages	31
Average weight of infants in this group	7 lb. 3 oz.
Median weight of infants in this group	6 lb. 14 oz.
Number of infants *with* retinal hemorrhages	16
Average weight of infants in this group	7 lb. 3 oz.
Median weight of infants in this group	6 lb. 10 oz.
B. FORCEPS DELIVERIES	
Number of infants *without* retinal hemorrhages	29
Average weight of infants in this group	7 lb. 5 oz.
Median weight of infants in this group	7 lb. 4 oz.
Number of infants *with* retinal hemorrhages	24
Average weight of infants in this group	7 lb. 10 oz.
Median weight of infants in this group	8 lb. 4 oz.

TABLE 5

EVALUATION OF DELIVERY

	No.	No. with Hemorrhages	Percent
Poor head control (spontaneous delivery)	10	7	70
Rotation of head with forceps	7	3	43
Oblique forceps applications	2	1	50
Multiple forceps applications	8	3	38

orrhages six hours and 45 minutes. Those deliveries that were spontaneous and examination revealed no retinal pathology had a mean duration of labor of three hours and 45 minutes while those mothers of babies in the group who manifested retinal hemorrhages had a mean labor time of five hours.

6. Evaluation of delivery technique

It is obvious that the degree of trauma inflicted on the infant varies with the skill of the operator as well as the conduct of labor. I was present at all deliveries so that a gross evaluation of the control of the delivery of the head as well as the presence of multiple or oblique forceps applications could be made. No record is generally made of the above aspects of the circumstances surrounding the delivery and consequently these have never been documented in their relationship with retinal hemorrhages in the newborn. The findings are charted in Table 5.

Poor control of the head in 10 cases was associated with retinal hemorrhages in seven or 70 percent of the group. Multiple forceps application occurred in eight cases, 38 percent manifesting hemorrhages; oblique forceps placement in two cases, 50 percent showing retinal hemorrhages and forceps rotation of the head in seven cases, 43 percent of those infants exhibiting the retinal hemorrhages.

TABLE 6

ANESTHETIC AGENTS EMPLOYED

	Cases	Cases with Retinal Hemorrhages (percent)
Saddle-block analgesia	57	42
Nitrous oxide-oxygen	33	33
Open drop ether	4	50
Caudal analgesia	3	66
Trilene, self-administered	2	50
None used	1	0

7. Anesthetic agents employed

Table 6 lists the anesthetic agents employed during the delivery, the number of cases in which each agent was used and the percentage of infants in each group who exhibited retinal hemorrhages.

The major agents utilized were saddle-block analgesia and a nitrous oxide-oxygen combination. Forty-two percent of those infants delivered with the aid of saddle block analgesia and 33 percent of those delivered under nitrous oxide-oxygen anesthesia manifested retinal hemorrhages.

8. Cyanosis of the newborn

In this series infants were considered to have an abnormal degree of cyanosis if they remained cyanotic greater than 15 seconds after delivery. Nineteen out of the 40 infants with hemorrhages and 18 out of the 60 without hemorrhages required greater than 15 seconds for the disappearance of cyanosis. Eight infants required greater than three minutes to become "pink," five of this group demonstrating retinal hemorrhages while three manifested no retinal pathology.

Comment

One of the more interesting aspects of the problem of retinal hemorrhages in the newborn is the great discrepancy between the different reports concerning its incidence. Several authors[14, 22] have attempted to ex-

plain the variations but none have statistically demonstrated the reason for the disparity. Differences in prenatal care, the use of vitamin K, and the method and time of the infant examination have all been suggested as possible factors explaining the varied percentages reported.

During the period of observation the level of obstetrics practiced and the prenatal care afforded the patients appeared to be more than adequate. It is, furthermore, unlikely that the percentage of hemorrhages in any series originating from a general hospital (as most recent series do) would vary to any large extent as a result of these factors.

Falls and Jurow,[7] in 1946, concluded that vitamin-K therapy administered to the mothers prenatally resulted in no lowering of the incidence of retinal hemorrhages in the newborn infant.

Assuming equal competence in the use of the direct ophthalmoscope the only factor (out of those factors previously enumerated) remaining as an explanation for the different percentages of hemorrhages in the newborn is the time of the examination of the infant after birth. In many of the published reports the time of examination is listed as "shortly after birth." Others state that the infants were seen within 24 or 48 hours while several groups used examination within three or four days as criteria for inclusion of an infant into their series.

It has been stated by many observers that several of the hemorrhages resorb within 24 hours, many by 48 hours and practically all within a week. The time of disappearance of hemorrhages in those infants examined in this series is listed in Table 7. As mentioned previously, all of the infants in this series were examined within one hour after birth. If, however, examination was delayed until 24 hours after birth a figure of 36 percent instead of the recorded 40 percent would have been given as the percentage of retinal hemorrhages in the newborn. Examination at 48 hours would have revealed a percentage of 25 percent and at 72 hours only 20 percent of the infants still demonstrated hemorrhages in the retina.

TABLE 7

TIME OF EXAMINATION AND PERCENTAGE OF HEMORRHAGES RECORDED

Hours After Birth	Percentage of Hemorrhages Found
1	40
24	36
48	25
72	20

Although the statistical significance of the figures in this series is low, it seems logical to assume that the major part of the explanation for the discrepancies reported in the literature is due to the variation in the time of the initial examination.

Most observers feel that obstetric trauma is the most probable cause of the retinal hemorrhages in the newborn. It is assumed by many that the trauma involved in the delivery of a primipara is greater than that in the delivery of a multiparous patient and further, that forceps application per se inflicts greater trauma to the head of the infant than would ordinarily occur in a spontaneous delivery. In this series, however, the differences in the percentage of retinal hemorrhages found in infants of multipara (38 percent) and primipara (45 percent) as well as the difference between those infants delivered spontaneously (34 percent) and those delivered with the aid of forceps (45 percent) is not very striking.

Because of the small differences in the aforementioned groups an additional finding bears mention as a possible factor in the production of retinal hemorrhages in the newborn. As the head is molded during the infant's passage through the birth canal, pressure is built up within the cranium and intracranial venous congestion and stasis results. This pressure is released with the delivery of the infant head over the perineum. The change in pressure—or pressure gradient—can be large or small depending on the rapidity or control of the delivery. Thus in a

well-controlled, slow delivery of the head the pressure gradient is small and the change from the high pressure of the birth canal to the low pressure of the perineum is gradual. Conversely, in a poorly controlled, precipitous delivery of the head, the pressure gradient is high and the cranium experiences a dramatic change from a very high to a very low pressure environment.

As a result of this high pressure gradient, diapedesis of blood and rupture of blood vessels may occur. It is therefore not surprising to find that out of the 10 infants listed as being delivered spontaneously with poor control seven demonstrated retinal hemorrhages (70 percent). The remaining 37 infants, delivered spontaneously with adequate control of the head, presented with hemorrhages in nine cases or 24 percent.

These findings suggest that the degree of head control and the rapidity of release of the intracranial pressure in the delivery plays an important part in determining the presence or absence of retinal hemorrhages in the newborn infant.

Asphyxia of the newborn has been implicated by some authors as a cause of the hemorrhages. This study did not corroborate this claim.

The length of labor, weight of the infant and anesthetic agents employed did not appear to influence greatly the occurrence of retinal hemorrhages in the infants examined in this series.

Neither in this paper nor in the literature can one find enough convincing evidence to implicate any single specific factor as the cause of retinal hemorrhages in the newborn. That a single, as yet undetermined agent, may exist cannot be denied, but in the light of present knowledge one must conclude that multiple factors are involved.

Summary and Conclusions

In an effort to determine the incidence of retinal hemorrhages, 100 newborn infants were examined no more than one hour after birth. These findings and the analysis of possible causative factors are reported.

The following conclusions were reached:

1. Retinal hemorrhages are a common finding in the newborn infant, occurring in 40 percent of the cases examined in this series.

2. The parity of the mother, weight of the infant, duration of labor, anesthetic agents employed, and degree of cyanosis at birth cannot definitely be implicated as major causes of retinal hemorrhages in the newborn.

3. Rapid release of the increased intracranial venous pressure as a result of poor delivery of the head of the infant seems to play a significant part in determining the presence of retinal hemorrhages in the newborn.

4. The variable time of the first ophthalmologic examination of the infant is the probable explanation for the great discrepancy in the reported incidence of retinal hemorrhages in the newborn.

University Hospital.

I wish to express my thanks to Dr. George Sayre and Miss Marguerite Lander and their staffs for co-operation in this study. The guidance and counsel of Dr. Harold F. Falls and Dr. Samuel J. Behrman is also gratefully acknowledged.

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THE MOVEMENT OF FLUORESCEIN AND WATER IN THE CORNEA*

D. M. Maurice, Ph.D.
London, England

On two occasions recently,[1,2] use has been made of estimates of the rate at which fluorescein passes across the corneal stroma. Underlying these methods is the assumption that a front face to the advancing dye may be sharply demarcated, and that its arrival at the opposite surface of the cornea can be timed with some precision (though estimates vary from about five min. in the first paper to one hr. in the second). The purpose of this note is to emphasize that these conceptions are mistaken and can result in erroneous conclusions being drawn. This has a certain importance because, in the first paper, it is suggested that the measurements of the passage time of fluorescein under various conditions could best be explained if there were a substantial flow of water out of the cornea across both its limiting surfaces.

* From the Ophthalmological Research Unit, (Medical Research Council), Institute of Ophthalmology.

Movement of fluorescein in the stroma

There is reason to believe that the movement of most substances within the stroma obeys the simple laws governing diffusion in uniform media. The behavior of fluorescein which enters the cornea can readily be calculated on this basis. The simplest case to consider is when some of the dye is liberated momentarily at one surface of the stroma and diffuses across to the other; this should correspond approximately to what happens when a drop of concentrated solution is instilled into the conjunctival sac and shortly afterward washed away. Figure 1 shows how the concentration varies across the stroma as the fluorescein spreads into it. The shape of the curve is that of the simple error or Gaussian curve, and is such that the concentration is given by:[3]

$$\frac{M}{\sqrt{\pi Dt}} e^{-x^2/4Dt}$$

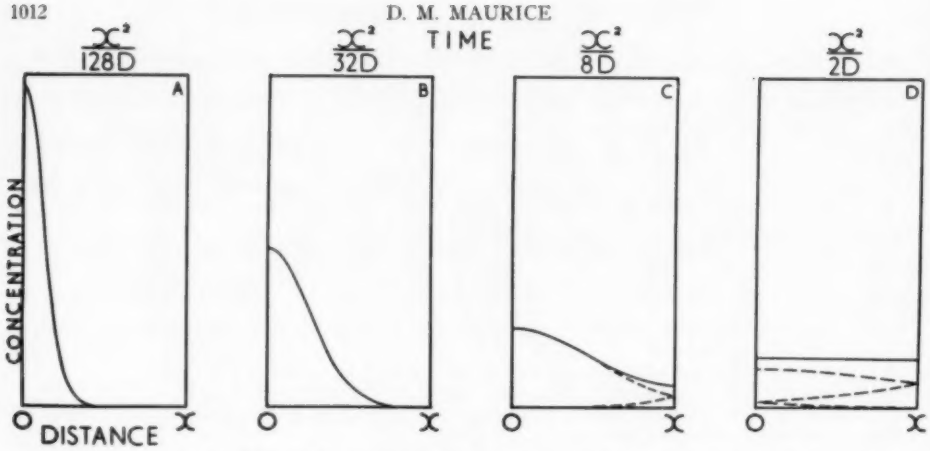

Fig. 1 (Maurice). Diffusion of fluorescein across the stroma. The sides of each panel represent the two faces of the cornea and the curve represents the distribution of fluorescein at four different times after its entry into stroma at left-hand face. Dotted line shows reflected simple diffusion wave; full line, actual concentration built up.

where t is the time after mass M of fluorescein was liberated over each unit area of cornea, and x is the distance into the stroma. D is the diffusion constant of fluorescein in the stroma, a quantity that expresses its rate of spreading and is expressed in units of cm.²/sec.

In each successive panel in the figure the dye has spread twice as far, corresponding to a diffusion time four times as long. The times, corresponding to the four stages represented, may be thought of as 0.5 min., 2.0 min., 8.0 min., and 30 min. extremely approximately. When the diffusion wave reaches a barrier, the epithelium or endothelium, across which relatively little of the dye is lost in the period under consideration, it is reflected as indicated in panels c and d by the broken line. The actual concentration is the sum of the incident and reflected waves and is shown by the full line.

The time course of the rise in concentration at the endothelial surface can also be derived from the formula, and it is shown in Figure 2, curve a. Fluorescein will gradually leak across the endothelium and build up a concentration in the aqueous humor. The total quantity which passes across can be obtained by the integration of curve a, and its growth is shown by curve b. Naturally, the dye will be lost from the anterior chamber by drainage, and the concentration in the aqueous humor will drop below that shown by curve b as time goes on.

In similar experiments, fluorescein may be brought into continuous contact with one surface of the cornea; for example, if a solution of the dye is injected into the anterior chamber.[1] Under these conditions the dye will be liberated at a steady rate at one surface of the stroma. Calling this rate Q per unit area, the concentration at a distance x within the stroma from this surface will be:[3]

$$2Q\left(\frac{t}{D}\right)^{1/2}\left\{\frac{1}{\sqrt{\pi}}e^{-n^2}-n(1-\text{erf } n)\right\}$$

where

$$n=\frac{x}{\sqrt{4Dt}};$$

how it varies within the cornea is shown by curve a, Figure 3. For comparison, curve b in this figure shows the variation in concentration that would be found if the same total quantity of fluorescein, Qt, was liberated at the beginning instead of gradually throughout the period, t.

The initial rise in concentration at any

point in the stroma, when the fluorescein solution is constantly in contact with one surface of the cornea, is identical in form with curve b, Figure 2.

Significance of visual estimates

It is evident that the gradual rise in concentration at the advanced edge of the spreading dye makes it impossible to define a time of arrival at any point or a distance travelled in any given time. The same difficulties apply to the appearance time in the aqueous humor or tears, as the case may be.

The apparent values will depend on the sensitivity with which fluorescence may be detected, and the total amount of dye which has entered the cornea, as well as on the diffusional properties of the stroma. The sensitivity may be limited either by the opalescence of the stroma itself, or by the intensity and color of the slitlamp light and the visual threshold of the observer, to mention only some of the possible variables.

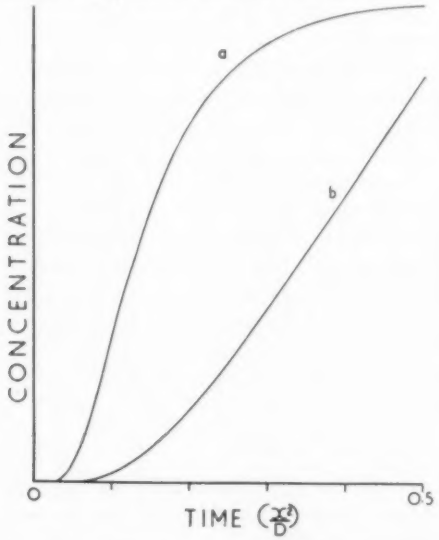

Fig. 2 (Maurice). (Curve a) Rise in concentration at endothelial face of cornea, after fluorescein is applied to epithelial face. (Curve b) Rise of concentration in aqueous humor. Ordinate is concentration in arbitrary units, different for the two curves.

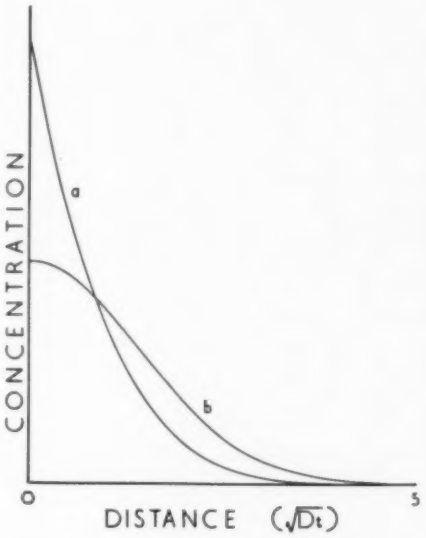

Fig. 3 (Maurice). Concentration profiles of fluorescein within the cornea after (curve a) passing continuously across face during time t, (curve b) same total quantity entered face at beginning of time t.

The amount of dye entering the cornea depends on, among other things, the concentration of the solution and the permeability and integrity of the cellular layer to which it is applied.

It is now possible to explain some of the observations of Beswick, et al.[1] For example, they found a more rapid movement outward across the stroma when the endothelium was damaged. In these circumstances a far greater quantity of fluorescein will enter the stroma than when the endothelium is intact. It can be seen from curve b, Figure 2, that if 10 times as much enters the stroma, for example, the front edge of the diffusion wave might be detected at the epithelial surface in half the time. The more rapid movement of the dye inward across the stroma which was observed when the epithelium was damaged will have a similar explanation.

The apparent[1] slowing down of the outward passage of fluorescein under a patch of denuded epithelium is less easily explained. Partly it could be caused by the

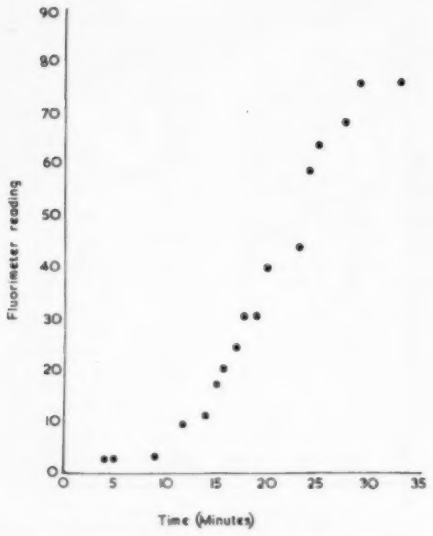

Fig. 4 (Maurice). Appearance of fluorescein in anterior chamber of a rabbit after its application to corneal epithelium.

swelling of the stroma in this area so that both the clear zone in advance of the spreading dye is broader and the light scattering of the tissue itself is greater. In addition, it is possible that the first traces of fluorescein arriving at the anterior surface are washed away by tears instead of being reflected by the epithelium; the reflected wave doubles the concentration in the region of the surface and can make a substantial difference to the visibility of the dye.

Objective measurements

I have made some objective measurements of the appearance time of fluorescein in the aqueous humor after its application to the anterior corneal surface. Some 10-percent fluorescein solution was applied to the corneal periphery of rabbits, either unanesthetized or under general anesthesia. After 10 to 20 sec. the surface was flushed with saline. A modified version of the fluorophotometer of Langham and Wybar[4] was focused on the aqueous humor behind the clear central area of the cornea and readings of the fluorescein concentration present in the fluid were taken at intervals. The results from one eye are shown in Figure 4.

The experimental values in the early stages should be comparable with the theoretical curve b, Figure 2. This curve has a nearly linear portion which, when projected downward, cuts the abscissa at a time $0.156 \frac{x^2}{D}$. Experimentally, this time varied between nine and 14 min. in five rabbits, with an average of 11 min. The average stromal thickness x was estimated from measurements taken of the total corneal thickness[5] to be 0.36 mm. The value of D thus is about 3.3×10^{-7} cm.^{2}/sec.

The results are consistent among themselves but they must be subject to systematic errors introduced by ignoring both the time taken for the fluorescein to pass the limiting corneal layers and the time taken for it to mix with the aqueous humor in the center of the anterior chamber. The diffusion rate across the stroma will, therefore, be underestimated.

In other experiments the rate at which fluorescein diffuses in the plane of the cornea was measured in vivo. A needle prick was made centrally in the corneal epithelium, and some concentrated fluorescein solution was brought into contact with the surface and then washed away with saline. This produced a local concentration of the dye in the stroma from which it spread evenly in all directions.

If a mass N of dye enters the stroma its concentration at a distance r from the needle prick after a time t will be given by:[3]

$$\frac{N}{4\pi Dt} e^{-Kt} e^{-r^2/4Dt}$$

where K is the permeability of the endothelium to fluorescein. At any given time the distribution of the dye will be in accordance with the error curve

$$e^{-r^2/4Dt}.$$

After a few hours each animal was killed and a central strip of cornea cut out. This

was mounted under oil and the distribution of fluorescein along it determined with the fluorometer. The results conformed adequately to the theoretical curve, Figure 5, and led to a range of estimates of D of $0.7 - 1.35 \times 10^{-6}$ cm.^{2}/sec. with a mean of 1.10×10^{-6}, in five experiments.

The value of the diffusion constant of fluorescein in free solution does not appear to be readily available in the literature. Some measurements were therefore made on diffusion of the dye into columns of agar gel; the agar did not appear to hinder its movement since identical results were obtained at gel concentrations of 2.0 and 0.5 percent. The agar was made up in saline buffered to pH 7.0 and the tubes were maintained in an incubator at 37°C. Four separate measurements gave values between 5.7 and 6.0×10^{-6} cm.^{2}/sec. for the diffusion constant.

The movement of fluorescein in the plane of the stroma appears to be slowed up a little over five times by the tissue. An exact figure cannot be given because of the variation in the results and the uncertainty of the corneal temperature in these experiments. However, this figures agrees well with those calculated[6] for the slowing of the movement of Na^{24} —five to six times, and heavy water—five times, across the stroma.

The estimate of the diffusion constant of fluorescein across the stroma, derived earlier, 3.3×10^{-7} cm.^{2}/sec., is 18 times less than its value in free solution. There is nothing in the structure of the stroma to explain such a small value compared to that found for movement in the plane of the cornea; hemoglobin has been observed[6] to move equally in the two directions. This value almost certainly is in error. Of the two possible causes of systematic error mentioned previously, it is probable that poor mixing in the anterior chamber is the more significant. This may give rise to a gross uncertainty in the estimate of the appearance time in the anterior chamber of fluorescein coming from the posterior chamber.[7,8] It is best that all conclusions drawn from experiments in which the appearance time of fluorescein in the anterior chamber is measured either subjectively or objectively should be regarded with suspicion.

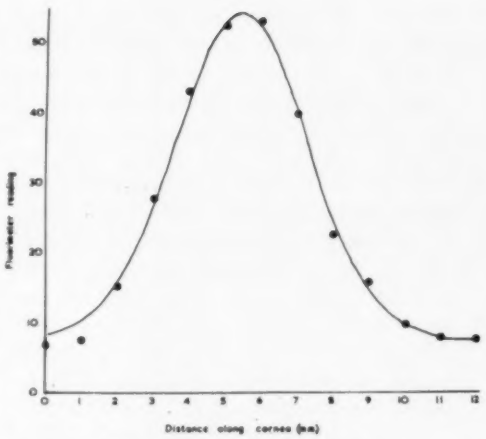

Fig. 5 (Maurice). Distribution of fluorescein around cornea 4.3 hr. after its introduction into stroma at central point. The circles represent measured values; they are fitted by a Gaussian curve with a standard deviation of 1.9 mm. and correspond to a diffusion coefficient of 1.15×10^{-7} cm.^{2}/sec.

Water movement in the cornea

Beswick, et al.[1] concluded that their observations on the movement of fluorescein in the stroma could be explained if there were a movement of water out of it across both surfaces. The necessary rate of flow they calculated to be about 2.5 mm./hr. across the epithelium and 5.0 mm./hr. across the endothelium. The surface area of the rabbit's cornea is 2.0 cm.^{2} so that this suggestion requires that 1.5 ml. of water must leave the cornea every hour across its surfaces. Since the cornea does not shrink, water must be entering across the limbus at the same rate. The circumference of the cornea is 5.0 cm. and its thickness 0.4 mm., and so its circumferential area is 0.2 cm.^{2} The rate of flow of water into the stroma at the limbus would therefore have to be 75 mm./hr.

If this flow of water existed, it should tend

to carry along with it all solutes capable of diffusing within the stroma. Gifford[9] found that no central displacement of the stain could be detected after fluorescein was introduced into the stroma through a peripheral scratch in the epithelium. I have confirmed this observation but it seemed that a less rapidly spreading substance would be capable of providing a more sensitive test for flow. The obstruction offered to the movement of proteins in the stroma is not much greater than that of fluorescein, yet because of their slow rate of spread the position of a localized concentration in the cornea can be determined over a longer period.

Accordingly, some concentrated hemoglobin solution was prepared from the blood of a blue-eyed rabbit and a very small volume was injected under the corneal epithelium of each eye about two mm. from the limbus. There was no tissue reaction, and the protein spread readily both across the stroma and in the plane of the cornea. Photographs were taken immediately and after several hours and no over-all drift of the colored spots was distinguishable; it was estimated that any such movement would be less than 0.1 mm./hr. It is unlikely that there can be a flow of water much greater than this across the limbus. The reasons for doubting that there is an appreciable flow of water across the corneal endothelium or epithelium have been noted previously.[10]

Although this experiment seems to deny the possibility of a substantial flow of water across the corneal surfaces, it should not necessarily be interpreted as evidence against an excretion of water by the limiting layers of the cornea. This active removal of water has been suggested as the mechanism by which the cornea maintains its normal thickness.[11] If the active excretion of water exactly balanced the amount which enters the stroma as a result of its swelling pressure, there would be no change in corneal thickness nor yet any appreciable flow of water at the limbus.

Summary

The movement of fluorescein experimentally introduced into the cornea and its use as an index of the flow of water through the stroma are discussed. It is shown that subjective and even objective estimates of its rate of movement can be in error. Evidence is presented against the existence of any appreciable flow of water within the cornea.

Judd Street, W.C. 1.

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KERATITIS AND DEAFNESS*

JOHN R. FAIR, M.D.
Augusta, Georgia
AND
GEORGE A. LEVI, M.D.
Fayetteville, North Carolina

The syndrome of nonsyphilitic interstitial keratitis associated with vestibuloauditory symptoms was described by Cogan[1] in 1945. Since then, numerous examples of this clinical entity have been reported. Oliner, et al.,[2] reviewed the literature up until the time of their case report in 1953. Additional cases recorded between 1953 and 1957 are referred to by Eisenstein and Taubenhaus[3] in a study of three patients with this unusual disorder.

With each new report it becomes increasingly apparent that keratitis and deafness are only the ocular and aural manifestations of a generalized hypersensitivity reaction. Still, the present state of our knowledge is such that any consideration of the subject must be limited to descriptions of individual cases with the hope that as information collects we may some day define the disease more clearly and perhaps develop a successful means of treatment.

It is the purpose of this paper to report three clear-cut examples of the syndrome as originally described by Cogan and, in addition, to record the results of an attempt to produce keratitis and deafness in laboratory animals.

REPORT OF CASES

CASE 1

A 25-year-old white man was inducted into the Army October 7, 1952. On October 22nd he was hospitalized with nausea and vomiting aggravated by standing and the complaint of staggering. He had had an upper respiratory infection for several days prior to the onset of these symptoms. He improved in the hospital and was discharged to duty but on October 30th noticed dizziness and a "stopped up" feeling in the head. At this time, hearing loss was first noticed along with tinnitus and he was readmitted to the hospital on November 10th. A staggering gait was noted. Urinalysis, serologic test for syphilis, chest X-ray films were negative. On November 25th, caloric stimulation with 30 cc. of cold water evoked no symptoms or nystagmus. Hearing was recorded as LCV AD 0/20, AS 0/20. Eight to 10 large superficial corneal opacities arranged in a circular fashion near the limbus were noted in each eye. On December 2nd, a lumbar puncture revealed no cells in the spinal fluid, sugar 60 mg. percent, chlorides 670 mg. percent, total protein, 44 mg. percent.

Past history included intermittent episodes of redness of the eyes for nine months prior to induction in October, 1952. There had been recurrent frontal headaches for the same length of time. The patient was a farmer and bulldozer operator. There was no history of familial disease.

Army immunization record was as follows: Smallpox vaccination October 20th. (There had been no prior vaccination to smallpox.) Triple typhoid vaccine October 9th, October 20th, and November 3rd. Typhus, November 6th. Cholera, November 6th, tetanus, October 9th and October 20th.

We first saw the patient January 11, 1953. Visual acuity was 20/30, O.U. There was marked photophobia and tearing. The conjunctival vessels were injected and there were noted numerous large round opacities in the superficial stroma of each cornea distributed fairly evenly in a circular fashion just inside the limbus. There were no cells or flare in the anterior chamber of either eye. Central and peripheral fields of vision were normal. Conjunctival smears showed only rare pus cells and a culture of the conjunctival secretions was negative. Deafness was complete. Local and systemic antibiotics, cortisone locally and systemically and beta radiation to each cornea all were without effect.

On March 2, 1953, there was an acute exacerbation of the keratoconjunctivitis and for the next two months the patient was never free of symptoms. In July, visual acuity was: R.E., 20/60; L.E., 20/30. There had been marked progression of the corneal opacities especially in the right eye where central infiltrates had developed.

In the next six months there was little change except that vessels were seen to have invaded each cornea for a distance of three or four mm. along its entire circumference. Central opacities were now described as being both superficial and deep.

On January 15, 1954, the patient suddenly developed severe vertigo, nystagmus, tendency to fall

* From the Division of Ophthalmology, Department of Surgery, Medical College of Georgia. Portions of this study were supported by a grant from the Knights Templar Eye Foundation.

forward and numbness of the right side of the face and left side of the trunk. Thrombosis of the right posterior inferior cerebellar artery was suspected. Lumbar puncture revealed normal pressure, two cells per high powered field and no increase in globulin. An electroencephalogram and skull X-ray films were normal. Two weeks later, a grade III, low pitched, rather harsh apical systolic murmur was heard for the first time. The murmur replaced the first heart sound and radiated generally over the precordium, into the axilla and posteriorly over the left lower chest. Fluoroscopy suggested a slight left ventricular hypertrophy. Electrocardiogram showed incomplete AV block.

The patient was then transferred to the medical service of the hospital. His weight had fallen from 160 pounds at the time of induction to 140 pounds. Temperature was normal or very slightly elevated during the day with elevations to around 100°F. at night. Heart rate was above 100 even during bedrest and was recorded at times as high as 120 per minute. AV block continued with PR interval never measuring more than 0.28 sec. The murmur persisted. Blood pressure was 120/70 mm. Hg in each arm reclining. The lungs were clear. There was no venous distension or edema. Peripheral pulses were normal. The abdomen was normal. Several small spider angiomas were present on the dorsum of each hand.

Complete blood count showed only mild anemia. Corrected sedimentation rate was 11. Differential white blood count was normal. Total eosinophil count was 50 per cu. mm. Urinalysis showed a trace of albumin and many red blood cells. Serologic test for syphilis was negative. LE cell prep, negative. Four blood cultures were negative. Bleeding time was recorded as 14 minutes, coagulation time, five minutes. Prothrombin time was 50 percent. Serum C assay was within normal limits. Liver function studies were normal. BUN was 12. Total protein was 7.2 gm. with a reversal of the AG ratio. Paper electrophoresis showed high levels of alpha globulin. Serum sodium 145, serum potassium 4.2. A 24-hour urine specimen showed urobilinogen 0.92 Eu/100 cc. and 10.7 Eu/24 hours.

Biopsies of skin and muscle were normal. An excised lymph node showed only reactive hyperplasia. Liver biopsy was reported as showing only minimal periportal infiltration of lymphocytes. Sternal marrow studies were normal.

Bacterial and viral cultures of blood and lymph nodes showed no growth. Excretory urogram and cystogram were within normal limits and barium swallow was normal.

Subsequently, the patient's general condition improved and he was discharged from the Army in June, 1954. Eighteen months later he reported by letter that his eyes were still giving him trouble at intervals and that his deafness remained complete.

Case 2

A 22-year-old previously healthy white man enlisted in the Army in March, 1951. After basic training, he was transferred to Alaska where he was hospitalized four times between January and May, 1953, with bilateral "acute conjunctivitis." At the time of the last hospitalization, he developed severe vertigo, deafness, and tinnitus. Deafness developed first in the left ear and within two weeks the right ear was involved. The deafness rapidly became total. The vertigo disappeared slowly. He was returned to the United States where the only ocular findings were minute circular superficial scars at the level of Bowman's membrane arranged along the circumference of each cornea just inside the limbus. There was no vascularization of either cornea and no iritis. Vision was recorded as 20/20, O.U. There was complete bilateral nerve deafness.

On April 10, 1954, a mild keratoconjunctivitis developed in each eye with photophobia, tearing and blurring of vision. Superficial corneal infiltrates were now noted in the central area of each cornea where none had been before.

This patient was subjected to the same extensive examinations listed in Case 1 including biopsies of skin, lymph node, muscle and liver. The results of all examinations were within normal limits. Inflammation of the eyes in this case has not recurred but hearing has not returned. He was last heard from in February, 1955.

Case 3

A 24-year-old white man, a native German who had enlisted in the American army, was admitted to an army general hospital in Germany because of acute vertigo, tinnitus, vomiting, nystagmus and staggering gait. He had felt slightly weak for the previous seven days and two days before had been given "drops" because his eyes hurt. There was a dull left temporal headache. General physical examination revealed no significant abnormality aside from a heart rate of only 50. Routine laboratory and X-ray studies were within normal limits. Skull X-ray films were normal as was electrocardiogram. Ear, nose and throat examination showed some hearing loss in the upper ranges bilaterally and dead labyrinth (no response to maximal stimuli).

Eye examination was not requested for one month after admission. At that time there was found a mild injection of the deep conjunctival vessels at the limbus in each eye. The corneal epithelium was intact. Arranged peripherally in each cornea were diffuse, poorly outlined infiltrates located in the posterior half of the stroma. In addition, there was a generalized disturbance of the corneal endothelium which gave the entire cornea a faint ground-glass appearance but did not interfere appreciably with vision which was 20/25 on the right and 20/50 on the left. The nystagmus described by the original examiner had disappeared. There was no sign of iritis. Ocular rotations, muscle balance and NPC were normal.

Additional history revealed the fact that in the previous two or three months he had suffered some redness of the eyes and photophobia. Both eyes had been affected and each attack lasted only one or two days.

Approximately six weeks after admission to the

hospital, the patient could hear his watch tick with his right ear for the first time since the onset of the symptoms. There was no impairment of hearing in the conversational range. His ocular and aural symptoms went on to subside completely and he was returned to duty. Laboratory workup including spinal puncture had been completely negative.

Two months later the same patient developed fever, backache and general malaise and was readmitted to the hospital. Two days earlier he had had pain in the right flank which radiated into the right lower quadrant of his abdomen. In addition to the fever, there was nonproductive cough, chills and loose stools. There were no eye complaints. Chest X-ray films showed a slight infiltrative process in the lower lobe of the right lung. This cleared within the next four days.

During the first 10 days in the hospital, temperature rose daily to 102°F. and 103°F. There was bilateral axillary and inguinal lymphadenopathy. White blood count was 19,000 to 24,000 with 75 to 80 percent polymorphonuclear leukocytes. Eosinophils accounted for only one to three percent of the white blood count. Serologic test for syphilis was again negative. There was no improvement on antibiotics and the patient was transferred to the surgical service because of the possibility of a subdiaphragmatic abscess. He was now running a low grade fever. No ova or parasites were found in the stools. On abdominal laparotomy, there was found an enlargement of the mesenteric lymph nodes which were somewhat matted about the root of the mesentery and could be palpated along the aorta as high as the diaphragm. Along the entire length of the small bowel were thickened patches 2.0 by 3.0 cm. in size located on the antimesenteric surface. The spleen was enlarged to twice its normal size. Many firm nodules could be palpated over the dome of the liver but these could not be seen through the liver capsule. A Meckel's diverticulum was removed along with a specimen of one of the thickened patches. A lymph node was removed from the mesentery and a Silverman needle used to biopsy the liver in several places and a wedge removed from the liver edge. Appendectomy was also carried out.

Portions of the lymph node removed at operation were used to inject a guinea pig. Pathologically, this same node showed only reactive hyperplasia and mild chronic granulomatous inflammation (minute granulomas composed of multinucleated giant cells and histiocytes). The appendix was not remarkable except that there was a conspicuous number of eosinophils in the lamina propria.

Pathologic examination of the biopsy specimens of bowel and liver were reported as follows:

"The lamina propria and submucosa exhibit several poorly defined, fairly large foci of pleomorphic cellular infiltrate. This latter often extends down to the muscular layer or involves the overlying mucosa which is ulcerated in some places (fig. 1). The infiltrate is diffuse without any distinct pattern, or forms varying sized granulomata. The predominant cell type is a neutrophilic poly. However, eosinophils

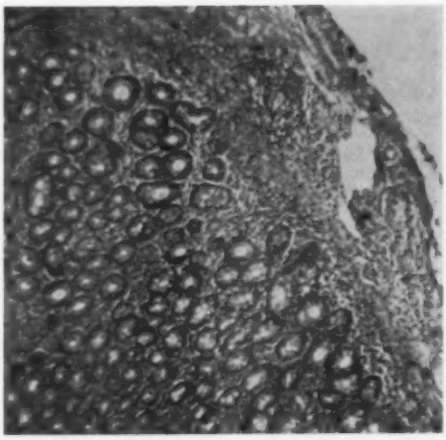

Fig. 1 (Fair and Levi). Ulcerative lesion in small bowel, *Case 3*.

are rather conspicuous. In addition, numerous plasma cells, lymphocytes, fibroblasts and histiocytes are noted. The latter are often of epithelioid nature showing palisade arrangement around central aggregates of acute inflammatory cells. Multinucleated giant cells are frequent in some areas. The subserosal tissues are edematous. The serosa is covered by a layer of fibrinous material containing numerous polys.

"Sections from liver show a few granulomata composed of unorderly arranged epithelioid cells, fibroblasts, histiocytes, lymphocytes and scattered eosinophils. Portal triads exhibit a rather prominent histiolymphocytic infiltrate (fig. 2).

"Diagnosis: (1) Ileitis, granulomatous, ulcerative, etiology undetermined; (2) reactive hyperplasia and mild chronic granulomatous inflammation, etiology undetermined, mesenteric lymph node; (3) Hepatitis, chronic, granulomatous, mild, etiology undetermined."

Following operation, a slight postoperative ileus developed which required the use of the Miller-Abbot tube. On one occasion, intestinal contents removed by the tube showed acid fast rods. On the basis of this finding and the granulomatous nature of the inflammation of the bowel wall removed at operation, antituberculous therapy was begun using streptomycin and PAS. Low-grade fever continued along with anorexia and occasional nausea. After a few days, the patient was transferred to the United States where his examination and treatment continued.

Upon his arrival in the United States, physical examination was essentially normal aside from tenderness in the right lower quadrant of the abdomen and in the left para-umbilical area. Serologic test for syphilis and routine urinalysis were negative. White blood count was 9,650 with a normal differential. Hemoglobin was 13 gm. Sedimentation rate 33 mm./hr. Hematocrit, 44 percent. Agglutina-

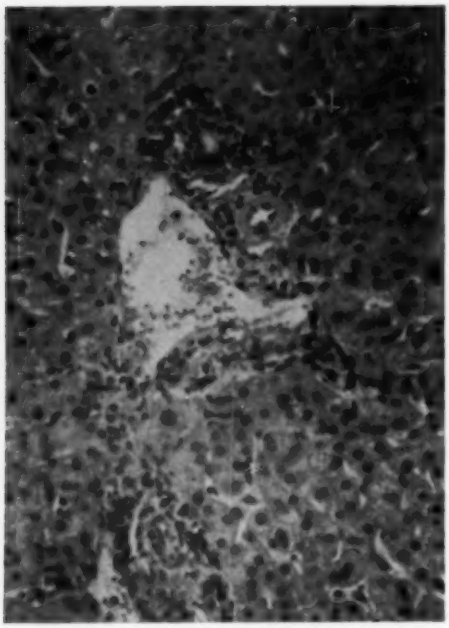

Fig. 2 (Fair and Levi). Section of liver, showing periportal infiltration of inflammatory cells, *Case 3.*

tion studies revealed a typhoid O titer of 1:160, H titer, negative. Proteus OX2, OX19 and OXK were negative. Five gastric washings were reported as negative on culture for acid-fast bacilli. Culture of a left axillary lymph node was reported as showing no growth. Total protein and AG ratio were normal. A follow-up report from the army hospital in Germany indicated that guinea pig inoculations done at the time of the original operation were negative.

Routine chest X-ray films were normal, long bone survey and X-ray films of the skull were negative. X-ray films of the esophagus, stomach, and duodenum were normal on two occasions. However, segmentation was noted in the small bowel which was interpreted as being compatible with abnormal motility but no intrinsic lesions were seen. Barium enema revealed no essential abnormality. Biopsy of the gastrocnemius muscle was negative. Liver function studies were normal.

A lymph node removed at this time was interpreted as showing only hyperplastic lymphadenitis. LE cell preparation was negative. Tuberculin skin test showed a plus-one reaction to first strength PPD. General condition gradually improved. He gained weight and subsequently was returned to duty.

Eye examination at this time revealed no evidence of inflammation of the cornea, past or present. There were no other ocular abnormalities.

Discussion

The three cases described follow closely the pattern of Cogan's syndrome established by previous reports. The subjects were previously healthy young males who suffered recurrent attacks of a peculiar type of interstitial keratitis followed shortly by vestibuloauditory symptoms including bilateral severe nerve deafness. In the first and third cases, it was obvious that the ocular and aural signs and symptoms were part of a systemic disease. In Case 1, periarteritis nodosa was suspected just as it has been in several cases reported previously.[3-5] Involvement of the gastrointestinal tract is not uncommon in periarteritis nodosa but there was no mention of changes in the blood vessels in the description of the chronic granulomatous inflammatory process seen in lymph node and bowel wall obtained at operation in Case 3.

An interesting observation which may some day shed light on this curious matter is a report by Hoekenga[6] on the development of keratitis and deafness in humans following the administration of Whipcide* (3 methyl-1-pentyn-3 yl acid phthalate) in the treatment of whipworm infestations. Ocular signs appeared 12 to 24 hours after ingestion of the drug and seemed to be related in degree of severity to the dose. Nausea and tinnitus were followed by slight to moderate deafness. Signs and symptoms lasted from one to three weeks.

Ocular manifestations of toxicity due to Whipcide are unknown in small animals according to the manufacturer of the drug although such signs have been noted in chimpanzees treated for whipworm with this preparation. Because specific information was lacking in this regard, several varieties of small animals were treated with Whipcide in this laboratory in an attempt to reproduce the keratitis described in humans. The drug has been administered to mice and rats by the oral and intraperitoneal routes, to rabbits

* Trademark, Pitman-Moore Company, Indianapolis, Indiana.

and cats by mouth and by vein and by mouth to one duck, one opossum and one rooster, all without effect on the eyes. Treatment of Whipcide by incubation with ground human liver did not alter its effect in this regard. These experiments by no means exhausted the possibilities of producing a combination of keratitis and deafness in animals using this drug.

SUMMARY

Three cases of nonsyphilitic interstitial keratitis with vestibuloauditory symptoms are reported along with the results of experiments aimed at the production of keratitis and deafness in laboratory animals by the administration of Whipcide (3 methyl-1-pentyn-3 yl acid phthalate).

Eugene Talmadge Memorial Hospital.

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THE LEAGUE AGAINST BLINDNESS

FERNANDO RODRÍGUEZ CONEJO*
Havana, Cuba

At the II Pan-American Congress in Montevideo, Uruguay, December, 1945, one important development was that each government adopt some sort of workable system for the prevention of blindness since science had already demonstrated that practically two thirds of all persons suffering from blindness could have been saved their misfortune had prophylactic measures been employed.

Dr. Tomas R. Yanes, who presided over the Cuban delegation, suggested the creation of an official organization for the prevention of blindness, together with a program for assistance to and protection of the blind, to be carried out through the Ministry of Health and Social Assistance. When he was unable to obtain the necessary backing, Dr. Yanes himself, in 1949, undertook the formation of a private institution, national in scope. To this various public and civic institutions generously gave their co-operation. And so the League Against Blindness came into being on September 7, 1951 (#15484, book 23, folio 46 of the register of Associations of the Provincial Government of Havana, Republic of Cuba).

The league, supported solely by private and public donations, has no political or religious segregation. Active members donate five dollars per year, guardians 10 dollars, benefactors 50 dollars. Those who donate a thousand dollars are considered life benefactors. Also there are members who pay regular monthly stipends.

The payment of these quotas is entirely voluntary, and does not obligate a person for

* Member of the School of Administration of Hospitals and Charity Institutions of the Republic of Cuba.

Fig. 1 (Conejo). Entrance to dispensary.

any length of time. The donor does not gain any economic advantage from his contribution, although he has the privilege of inspecting the administrative operations, and also has the chance to be elected to a responsible position.

Although during its first year the institution received less than three thousand dollars, it decided to find a dispensary for poor and sick people and on January 3, 1953, the first hospital was opened. With only eight beds, four doctors, three nurses, and five employees, this temporary establishment served for four years before it was almost forced to close because of lack of adequate facilities. However, the government provided adequate grounds and enthusiastic help from private citizens made possible the erection of a suitable dispensary, completed in April, 1957, at a cost of $222,416.09. The happy spirit in which this work was carried out, due in a large part to the founder of the league, was further demonstrated in 1956 when donations totaling $188,984.24 were received.

After the dispensary was finished, construction of a new building (also made possible by donations) was begun on May 12, 1957. The success of this undertaking was so great that, in 1958, the institution received voluntary donations totaling $293,904.35. The newspapers generously collaborated with the project. The number of doctors, nurses and employees had by now risen to 123, including personnel from the School of Ophthalmology.

The League Against Blindness is trying hard to reduce the number of blind persons and to alleviate the economic burden of the community that they represent. The personnel of the institution works under trained leadership and each patient receives careful examination, not only of the eyes but a complete examination, to find and treat other conditions that might endanger health. In this way preventive therapy against blindness is also instituted. For numerous young doctors working with these patients provides invaluable experience.

The dispensary of the League Against Blindness has 38 beds and houses all patients

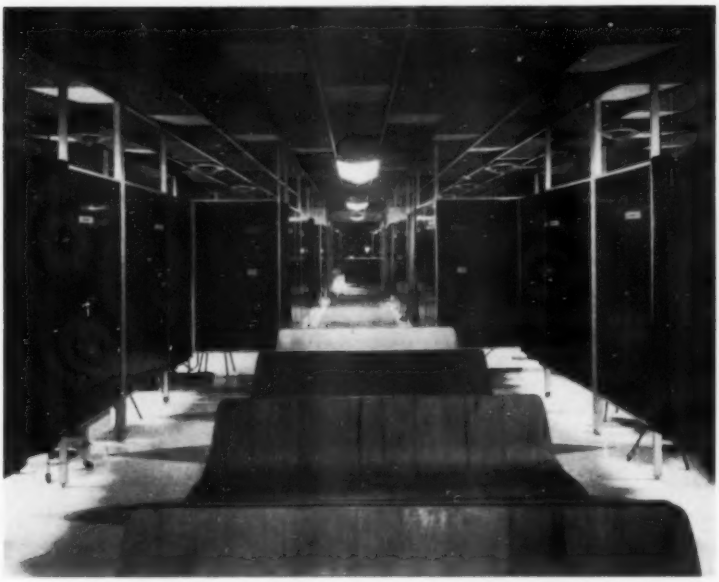

Fig. 2 (Conejo). Ophthalmologists' offices in dispensary.

until the actual hospital is completed. It is staffed by 30 specialists who attend to more than 200 sick persons daily. It is equipped with indirect music, air conditioning, and an intercommunication system. It has been paid for entirely by donations. Equipment and furniture, of the latest and most functional design, was selected for maximum efficiency.

The building itself will cost more than a million dollars, which must also be raised by donations. Construction has been under the able direction of the young architect, Emilio Fernandez. The hospital will contain patient rooms, kitchens, cafeteria, offices, and so forth, and many laboratories. The entire plant is divided into three sections: the dis-

Fig. 3 (Conejo). Hospital under construction.

pensary, now functioning with 38 beds, the hospital, under construction and with a capacity of 120 beds, and a conference section which is connected to the main building by a tunnel.

In 1956, Dr. Yanes established an academic and international organization called The Foundation for the Teaching and Development of Ophthalmology (Fundación para la Enseñanza y Desarrollo de la Oftalmología F.E.D.O.), which offers scholarships each year to graduate medical students.

Unfortunately the majority of medical students have lacked courage to tackle the problem of graduate study, which is a long and expensive process. The Foundation makes loans which can be paid back after the student completes the program and his financial situation permits him to do so. To be accepted an applicant must submit proof of: (1) the title of doctor of medicine; (2) good conduct; (3) a license to practice in his respective country; (4) to be under 35 years of age and to have received his M.D. degree less than five years earlier; (5) a working knowledge of the Spanish language.

After two years of intensive training and extensive eye surgery, a diploma is issued. Representatives from various Latin American countries have come to the school. All student doctors reside at the hospital. While the medical work that they do is important, the educational program is even more so.

Everyone in Cuba has helped the League Against Blindness in whatever way they could. Thanks to them, in 1958, a total of 65,005 consultations were held, and 1,887 eye operations performed. A total of 1,361 patients (consuming 12,870 meals) were processed, in spite of the fact that the hospital is not yet finished. The people still continue to donate funds to keep the organization alive and functioning. In this way the league is able to continue its valuable work for the prevention and cure of blindness.

The example has been followed in other countries as well. Guatemala has just inaugurated a similar institution.

Oculists of the Western Hemisphere are cordially invited to participate in this work. The Cuban organization promises to help any country that desires assistance with this medical and social activity.

P.O. Box 86,
Marianao, Cuba.

EXPERIENCES WITH SURGERY AND STRONTIUM-90 IN THE TREATMENT OF PTERYGIUM*

MARTIN BERNSTEIN, M.D.,† AND SOL M. UNGER, M.D.
Bronx, New York

The use of beta radiation in the treatment of certain superficial tumors and lesions of the eye has become an established method of treatment.[3] Four years ago the Bronx Veterans Administration Hospital obtained a strontium[90] applicator which has been used by the Eye Service in the treatment of various eye diseases. Various authors have expounded their results.[2,3,5,7,9] This paper is limited to experience with pterygia. Most published reports on radiation therapy of pterygia have been limited to six-month follow-up studies, possibly because of the difficulty in obtaining regular return visits to follow-up clinics. The follow-up of patients at this hospital fortunately has been successful and regular.

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* From the Ophthalmology Service and the Radiotherapy Service, Veterans Administration Hospital.
† Present address: 8 South Moger Avenue, Mount Kisco, New York.

Surgical material and methods

Most patients were of Puerto Rican or Cuban descent. All were males of military age. Pterygia occurred in patients of Mediterranean and other tropical heritage born in temperate climates. Some patients stated that their children were born with fleshy growths similar to their own.

A comparison of various surgical procedures was made. These fell into basic types: (1) transplanting procedures, (2) excision with total closure of conjunctiva, and (3) excision leaving bare sclera.

The greatest number of recurrences resulted from the transplanting procedures. There were fewest recurrences of true pterygia with the bare sclera technique, a description of which follows:

The head of the pterygium is dissected smoothly from the cornea to the level of Bowman's membrane. Special care is taken to avoid perforating the cornea if there has been previous surgery. The head, neck, and a portion of the body of the pterygium are excised including the subconjunctival and episcleral tissues. The conjunctiva retracts of its own elasticity, leaving an arc of cut conjunctiva approximately four mm. from the limbus at its greatest distance. This leaves a small area of bare sclera.

Sutures are not ordinarily used because of their irritating qualities and because a further irritating procedure is necessary to remove them. Sutures are occasionally used when complete removal of the pterygium results in too large an area of bare sclera. Subconjunctival (fig. 1) and scleral (fig. 2) epithelial cysts have occurred, possibly from implantation or epithelial downgrowth along the track of silk sutures.

Fig. 1 (Bernstein and Unger). A subconjunctival epithelial implantation cyst.

Fig. 2 (Bernstein and Unger). A scleral epithelial implantation cyst.

Patching the eye daily until complete epithelization has occurred produced a much faster subsidence of postoperative reaction. The use of topical steroids also reduced postoperative reaction and granulation.

Radiation technique

The strontium^{90} applicator is a readily available commercial product containing a 50 mc. source of strontium^{90} which has a half-life of 25 years. It gives a dose rate of 50 r beta equivalent per second at the surface of the applicator. The source has an active diameter of 7.8 mm. and an overall diameter of 12.7 mm. and is mounted on the end of a 6.75-inch shaft. A circular plastic shield, four inches in diameter and 0.25-inch thick, is mounted on the shaft. This shield may be moved to any desired position along the shaft, and will stop virtually all the radiation emitted by the source. The source it-

TABLE 1

SURVEY OF PTERYGIUM CASES

Total no. patients		49
Total no. operations		73
Total no. radiation treatments		49
Total no. eyes operated and irradiated		46
a. With bare sclera technique	39	
b. By other surgical techniques	7	
No. eyes with one or more recurrences before treatment		33
a. With surgery and irradiation	25	
b. With surgery alone	8	
Total no. eyes operated and not irradiated		27
a. With bare sclera technique	11	
b. By other surgical techniques	16	

self is protected by a double hermetic seal and is covered by two mils of stainless steel and ten mils of aluminum.

The radiation emitted by the source consists of 0.537 mev. beta rays, through which strontium^{90} decays to yttrium,^{90} and the 2.18 mev. beta rays through which yttrium decays to stable zirconium.

Published reports by Krohmer[6] show that the radium D and E applicators emit energies which are 90 percent absorbed in the first millimeter of tissue, whereas with strontium,^{90} 59 percent is absorbed in the first mm. of tissue, allowing 41 percent to penetrate to 3.0 mm. to tissues which we do not want to treat. Despite this, we prefer the strontium^{90} applicator because of its longer half-life, absence of gamma radiation, and ease of calibration. This simplifies the facilities and training needed, making the strontium^{90} applicator the most convenient beta-ray emitter for use by the ophthalmologist. It can be purchased from several commercial sources, but authorization is necessary from the United States Atomic Energy Commission.

The average pterygium treated with beta radiation may subtend an arc of limbus slightly larger than the diameter of the radio-autograph of the strontium^{90} applicator. When several applications are needed to cover the treatment areas, care is taken to avoid overlapping treatment areas. Those pterygia which are irradiated without surgery are treated at the limbus with the portal of the applicator overlapping the head of the pterygium. Those pterygia also treated surgically have the applicator applied to the cut edge of the conjunctiva and not the cornea. In this respect, the design of an applicator with arc shaped portals should be an improvement. Originally, dosage was given for a total of 4,000 rep divided in weekly doses of 1,000 rep. Some patients were referred to our hospital who had received dosages up to 5,000 rep at other institutions. At present we consider 3,000 rep to be sufficient. Where the slitlamp demonstrates the cornea to be thinned by previous surgery, radiation is reduced to 2,000 rep to avoid possible lens changes.[8] The large, fleshy, vascular, rapidly enlarging, recurrent pterygium requires 4,000 rep.

Radiation therapy was initiated at postoperative intervals varying from the day of operation (on the operating table) to as long as one month postoperatively. The best results occurred when radiation began before the fourth postoperative day. The most practical time to begin treatment is on the first postoperative day, at the change of dressing. This is better than at the time of surgery because there is a delay of many hours after the operative trauma before tissue cells begin to grow and reach a radiosensitive stage.

RESULTS

The hospital records were reviewed for four years and the data correlated according to (1) the type of surgical procedure, (2) the amount of radiation treatment and (3) short and long-term results and correlation of the above with recurrences.

Admittedly, the number of cases are too few from which to draw statistically valid

TABLE 2

RECURRENCES WITH SURGERY ALONE

Techniques	No. Cases
All surgical	16
Bare sclera	4
Other surgical	12

conclusions. However, Tables 1 to 4 are presented to demonstrate the basis from which some of the conclusions are drawn.

There were fewer recurrences of pterygia with the bare sclera surgery alone (table 2) than with other surgical techniques. The incidence of recurrence is still lower when followed by radiation therapy (table 2). No recurrences occurred in patients who were treated with strontium^{90} within four days postoperatively. Those irradiated patients who developed recurrences began beta-ray treatment after the fourth postoperative day.

TABLE 4

DURATION OF FOLLOW-UP

After Treatment	Six Months or Less	Six Months to One Year	One to Four Years	Over Five Years
With surgery alone	4	—	9	3
With surgery and Sr^{90}	15	2	29	—
With Sr^{90} alone	—	—	6	—

COMPLICATIONS

The side-effects of radiation therapy at dosages of 4,000 rep or more have been decribed elsewhere.[7] We found that dosages of 3,000 rep or less produced no visible side-effects by our methods of observation which included gonioscopy, slitlamp examination of the anterior segment, scleral depression and indirect ophthalmoscopy, over a four-year period. Immediate reactions have been described at higher dose levels than we have used.[10] However, we feel that photophobia, itching and burning, lacrimation and punctate keratitis can be due to the mechanical and chemical trauma received during radiation therapy and can also be duplicated by the postoperative reaction.

Experience with various surgical techniques brought out an interesting observation —some recurrences are not true pterygia but a form of pseudopterygium. Certain surgical techniques contribute to their formation.

If removal of the pterygium is followed by suturing the cut edges of conjunctiva together or to the sclera so as to cover all exposed sclera, then the conjunctiva often adheres to the cornea. This always happens when a superficial keratectomy removes Bowman's membrane and edematous conjunctiva overlaps the exposed corneal stroma. From this point there is a race between epithelization of the remaining raw cornea from adjacent corneal epithelium and from the conjunctiva

TABLE 3

RECURRENCES WITH SURGERY AND RADIATION

Techniques	No. Cases
Bare sclera	None
Other surgical	3

The relative nutrition of these two sources is an important factor in the formation of pseudopterygia. Much of the nutrition of the corneal epitheluim is derived from adjacent conjunctiva at the limbus. If a large area of conjunctiva is cut away, especially along a large arc of limbus, the nourishment of corneal epithelium is interfered with, and regrowth of conjunctiva onto the raw cornea occurs faster than epithelization of the corneal wound from intact adjacent corneal epithelium. Innervation of the cornea also is a factor in epithelization and proper nutrition.

Injury to the sources of the neural and vascular supply of the denuded cornea in the adjacent sclera by surgical trauma and the use of chemical and electrical cautery also interfere with the healing of the epithelium from the corneal side. The end-result is delayed epithelization of the cornea from the cornea, local edema of the cornea in the operated area, local anesthesia and neurotrophic disturbances with localized vascularization of the corneal stroma.

These injuries are probably a large factor in the massive recurrence of a pseudopterygium with or without superimposition of a true pterygium. This pseudopterygium does not grow once the cornea is healed, does not have a tunnel beneath it, and does not re-

tract. No pseudopterygium occurred with the bare-sclera technique.

The lens is the most radiosensitive of the ocular tissues. It is avascular and has poor reparative powers. Since clinically observable radiation effects may be delayed for months or years, one may be led to give additive doses to the lens in the treatment of multiple recurrences. For these reasons, a single course of treatment above 4,000 rep should not be repeated.

The results of this study suggest that radiation will reduce the incidence of recurrent pterygium when routinely used following surgery. Surgery, and in our hands bare-sclera surgery, produces excellent results with few recurrences. Therefore beta radiation is recommended when surgery fails, either alone or with reoperation as the case demands.

Discussion

Pterygia less than 0.5-mm. thick, not scarred, growing rapidly, highly vascular, extending less than 1.0 or 2.0 mm. onto the cornea, respond equally well to either bare-sclera surgery or radiation.

Large pterygia more than 0.5-mm. thick, heavily scarred, growing slowly or not at all and extending more than 2.0 mm. onto the cornea are poor candidates for radiation therapy with or without surgery.

Recurrent pterygia, not operated previously by bare sclera technique, deserve such technique first before resorting to radiation.

It is recognized that the most objective method for evaluating the benefit of postoperative radiation is by randomizing patients with bilateral pterygia of similar character. One eye is irradiated and the other not. However, such a study has not been reported and would be beset with varied difficulties, such as the infrequency of bilaterality of 25 percent, and further the infrequent finding of lesions similar in size, thickness and activity. Nevertheless, we believe that our clinical experience merits presentation. Of particular interest is a relatively small group of eight operated patients with bilateral lesions in whom only one eye was irradiated. Seven patients were observed after treating one eye with bare sclera surgery alone and the other with surgery and irradiation. One patient with binasal and bitemporal pterygia was similarly treated. This group of patients were followed for four years, and their results lend weight to our general conclusions.

It is of interest here to review a series of observations concerning the size, depth, and age of blood vessels that can be obliterated with strontium^{90}. We feel that growing capillaries that are superficial, especially in a budding stage, are easily obliterated by 2,000 rep. Capillaries more than four days' old, which are superficial, are moderately damaged, and the area blanched by 2,000 to 3,000 rep. Vessels which are just visible with the lower power slitlamp objectives, and are old and superficial, are difficult to destroy with doses between 4,000 and 7,000 rep. Vessels which are just visible to the naked eye whether new or old, superficial or deep, are almost impossible to destroy with dosages under 7,000 rep. Dosages over 7,000 rep cause local necrosis, paradoxical neovascularization and are dangerous to the lens.[7]

Summary

Methods and results of the surgical and strontium^{90} beta-ray therapy of pterygia are presented and discussed. A total of 3,000 rep divided in weekly doses is adequate treatment for the average pterygium or recurrence. Indeed, 4,000 rep or more does not produce better results, and 3,000 rep has not produced any complications. After removal of recurrent pterygia with marked thinning of the cornea from keratectomy, surface doses of 2,000 to 2,500 rep should not be exceeded, in order to protect the lens.

The previously untreated pterygium is best treated by surgery alone.

Strontium^{90} radiation reduces the incidence of recurrent pterygium following surgery and is best reserved for the treatment of surgical recurrences.

The bare-sclera surgical technique avoids the formation of pseudopterygium.

Patients receiving strontium^{90} therapy for pterygia should be observed for a minimal period of four years.

130 West Kingsbridge Road (68).

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Ophthalmic Miniature

Sir W. R. Wilde (Oscar's father) describes in the *Medical Times and Gazette,* February 1, 1868, a hitherto undescribed epidemic, which has recently prevailed in Ireland. . . . The disease reminds one of irido-chroiditis accompanying cerebro-spinal meningitis.

Dr. G. Hay,
Report of the Progress of Ophthalmology for 1867,
Tr. Am. Ophth. Soc., 1:5th meeting, 16, 1868.

NOTES, CASES, INSTRUMENTS

A SIMPLE OPTICAL AID*

FOR OBTAINING CALIBRATION CURVES IN TONOGRAPHY

MARGUERITE A. CONSTANT, PH.D.
AND
JAY ENOCH, PH.D.
Saint Louis, Missouri

Repeated calibration of the electronic tonometer by means of specially mounted micrometers is essential for reliable tonometry and tonography. Misreading the micrometer† vernier by the width of the line markings on the vernier may result in an error of some 13 percent of a scale unit on the upper portion of the scale and some 25 percent of a scale unit on the lower end of the scale. Although in practical tonography, this error may not be large, it is unnecessary. It is primarily due to the small size of the vernier and its spacings and the parallax which develops in attempting to read the gauge when it is set at the convenient height of a table. This difficulty has been overcome by the simple means described in Figures 1 and 2. The reproducibility of the calibrations

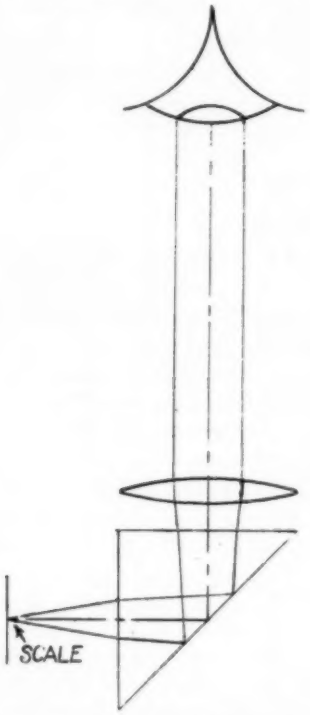

Fig. 1 (Constant and Enoch). Optical system of device for the micrometer.

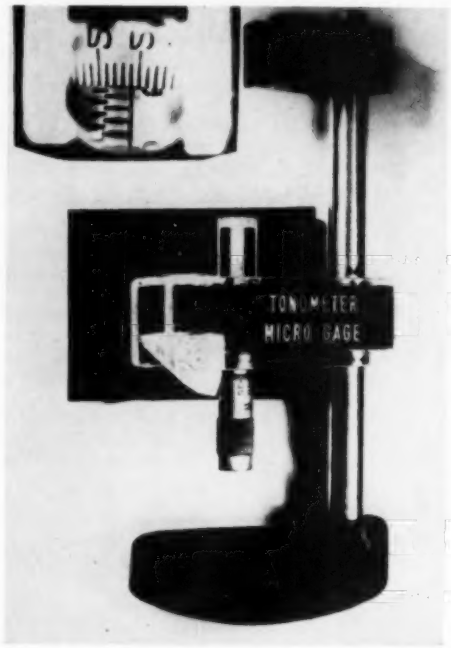

Fig. 2 (Constant and Enoch). Micrometer and stand with right angle prism and convex lens in place. Insert demonstrates image seen through the lens.

* From the Department of Ophthalmology and the Oscar Johnson Institute, Washington University School of Medicine. Supported in part by a research grant, B-621, from the National Institute of Neurological Diseases and Blindness of the National Institutes of Health, U. S. Public Health Service. We wish to acknowledge gratefully Mr. William Moor's assistance with the photography.

† Hillcrest Engraving Co., Mayfield Heights, Ohio.

during the day, and from day to day, have become uniformly excellent and the technicians are pleased with the convenience provided by allowing readings to be made under magnification (provided by the lens) and without awkwardly tilting the head to read the micrometer scale (provided by the prism). The greater constancy in the viewing angle and increased magnification probably account for the increased reliability.

The device consists of a right-angle prism glued to the arm supporting the micrometer, and an approximately 14 diopter convex lens conveniently positioned and held in place by two pieces of plastic glued to the sides of the supporting arm of the micrometer (figs. 1 and 2).

This system may be made as elaborate as desired. However, the present device is easily made from inexpensive materials that are readily available to most laboratories.‡

640 South Kingshighway (10).

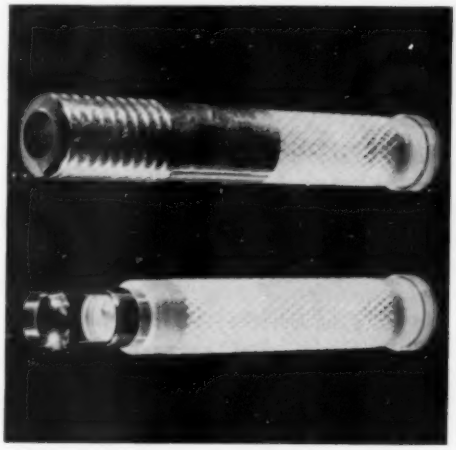

Fig. 1

‡ A modified detachable device is available from Ostertag Optical Service, 3851 Washington Avenue, Saint Louis, Missouri.

A CORNEAL TREPHINE*

WITH BUILT-IN OPTICAL CENTERING DEVICE

R. TOWNLEY PATON, M.D.
AND
MIGUEL MARTINEZ, M.D.
New York

The new corneal trephine (fig. 1) has three main advantages: simplicity of design, a high degree of visibility made possible by the design of the blade, and a built-in optical centering device.

The trephine itself has just two parts—a plastic handle and a stainless steel blade. There are no movable parts or complicated mechanisms to grow stiff or get clogged.

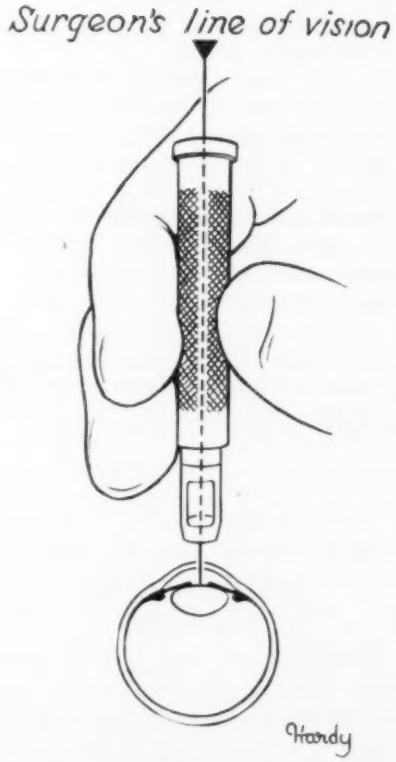

Fig. 2

* From the laboratory of The Eye-Bank for Sight Restoration, Inc., Manhattan Eye, Ear and Throat Hospital. Aided by a grant from the Knights Templar Eye Foundation. Manufactured by Storz Instrument Company, Saint Louis, Missouri.

The large slots in the side of the short blade permit the surgeon to see the exact angle and position of the blade in relation to the cornea. Even after the blade has been placed and while the cut is being made, the surgeon can see the corneal disc and gauge the depth of the cut.

The optical centering device consists of concave-convex optical surfaces which are ground on the two ends of the plastic handle, giving the magnification of about 6.0D. In centering the trephine, the surgeon fixes the eye routinely, then aligns the trephine grossly over the pupillary area close to the surface of the cornea (fig. 2). He can then sight the pupil through the barrel of the handle and place the trephine exactly. If an off-center graft is necessary, the surgeon can make a pin prick in the center of the portion to be removed, stain with fluorescein, and center the trephine over the mark instead of over the pupil.

The instrument should be sterilized in a nonalcoholic, cold solution, such as Zephiran or aqueous Merthiolate, since heat or alcohol would damage the plastic and spoil the optical surfaces.

A blade protector is supplied with the trephine which permits sterilization of the instrument with the protector in place.

210 East 64th Street (21).

FOOTNOTE

This trephine is a tribute to the mechanical skill of Dr. Martinez, who made the first models himself. I have been using it with great satisfaction and feel that it is a valuable advance. R. T. P.

A NEW CONCEPT OF THE GLAUCOMA PROBLEM*

PAUL WEINSTEIN, M.D.
Budapest, Hungary

During the past 10 to 15 years, data on the incidence of attacks of acute glaucoma have appeared in the ophthalmic literature of several countries. Bonavolontá has reported that acute glaucoma occurs frequently in Italy. Personal communications from Rosengren and Bárány state that such attacks seldom occur in Sweden. In Hungary, I found that acute attacks occur in about 20 percent of glaucomatous cases.

These data pose the question: What is the actual reason (reasons) for this difference. In my opinion the answer may be found in two etiologic factors—predisposition (narrow angle) and a highly unstable central nervous system.

During 760 gonioscopic examinations, I found that in 50 percent of subjects not afflicted with glaucoma, the angle was of normal width; in 25 percent it was narrow; in the remaining 25 percent it was wide. From these data it may be concluded that in about 25 percent of the population the angle of the anterior chamber is narrow, which would predispose these persons to glaucomatous attacks. It may be that, in those countries where acute attacks of glaucoma are more rare, the incidence of narrow angles is smaller.

It is also known that, in southern countries, the people have more volatile dispositions and their nervous systems are more easily irritated. This observation may help to explain a higher incidence of acute glaucoma in southern countries.

Diabetes and tabes also have an influence on the incidence of glaucoma. According to Bárány and to François, mucopolysaccharides are found in the trabecular meshwork. Hyaluronidase increases angle permeability, resulting in increased aqueous outflow.

Vascular changes in diabetes result from pathologic permeability of the blood vessels because of changed mucopolysaccharides. This knowledge prompts the supposition that, in diabetic patients, the polysaccharides of the trabecular meshwork undergo the same pathologic changes as those of the blood vessels, increasing the permeability of the angle. This may explain the low incidence of glaucoma among diabetics. In the

* From the Eye Department of the Medical Postgraduate Institute of Szabolcs Street.

examination of 1,000 glaucoma patients, I found only 20 suffering from diabetes—five had had acute attacks; 15 had chronic inflammatory glaucoma.

The iridoplegia of tabes dorsalis is, according to Apter, based on some localized nervous lesion. Apter cites the theory of Langworthy and Ortega which assumes that, in lues, some vascular lesion produces atrophy of the iris, with resulting destruction of the nerves. My studies show that degeneration takes place in the neurovascular cells of the ciliary ganglion. This observation would seem to explain why glaucomatous attacks never develop in eyes in which the iris has been destroyed. From this it may be concluded that tabes reduces the incidence of glaucomatous attacks. My statistics bear out this observation. Among 1,000 glaucoma patients were found only 10 cases of tabes—six of chronic inflammatory glaucoma; four of glaucoma simplex. No attack of glaucoma was observed in any of the 10 cases.

V. Balassi Bálint u. 9/11.

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CYCLOMYDRIL*

A NEW MYDRIATIC AGENT

BRUNO S. PRIESTLEY, M.D.
MYER M. MEDINE, M.D.
New York

AND

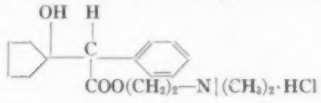
CARLTON C. PHILLIPS, M.D.
New Haven, Connecticut

In our original paper[1] introducing Cyclogyl* the clinical study was divided into two phases. In the first phase we reported the mydriatic effect of the drug. The second phase dealt with the cycloplegic effect of Cyclogyl and this aspect has been the subject of many subsequent reports.[2] Our forecast that Cyclogyl was destined to supplant homatropine in the routine practice of refraction has been borne out.

More intensive studies of this drug during the past five years have confirmed our initial findings of its usefulness as a mydriatic. The effect of the drug was studied in various dilutions alone and in combination with phenylephrine hydrochloride on 230 patients. These were subdivided into three groups, white patients with dark irises, white patients with light irises and Negro patients. Measurements were made as in our first report with a simple pupillometer of the Morton type. These results are shown in Table 1.

The maximum mean increase in pupillary size was obtained with a mixture of equal parts of Cyclogyl (0.2 percent) and phenylephrine (1.0 percent*) It was found to be the fastest acting and the most effective. Furthermore comparison studies with other mydriatics in current use such as ephedrine (5.0 percent), paredrine (1.0 percent), phenylephrine (2.5 percent and 10 per-

* Previously designated Compound 75G.T. Cyclogyl hydrochloride, brand of cyclopentolate hydrochloride, is a synthetic compound, B-dimethylaminoethyl (1-hydroxycyclopentyl) phenylacetate hydrochloride, having the following structural formula:



* This mixture is now designated Cyclomydril and is produced and distributed by Schieffelin & Co., New York.

TABLE 1

INCREASE IN PUPIL SIZE IN MM. 30 MINUTES AFTER INSTILLATION OF DRUG

	White Patients Dark Irises	White Patients Light Irises	Negro Patients	Mean Increase
Cyclogyl 0.1%	1.81	2.19	1.67	2.06
Cyclogyl 0.1%-phenylephrine 0.25%	3.02	3.94	1.75	3.16
Cyclogyl 0.1%-phenylephrine 0.50%	3.23	3.92	2.94	3.50
Cyclogyl 0.1%-phenylephrine 1.00%	3.11	4.54	2.65	3.57
Cyclogyl 0.2%-phenylephrine 1.00%	3.15	4.38	3.50	3.66

cent) and with a mixture of equal parts of phenylephrine (5.0 percent) and eucatropin (5.0 percent) demonstrated its greater effectiveness.

It is not possible to state at this time whether Cyclomydril's quick action is due to a synergistic effect or to a summation of the combined effects of the two drugs.

Intraocular pressure was carefully observed. Tonometric readings were taken before instillation of Cyclomydril and at the time of maximum mydriasis. Variations were generally nil in Negro eyes. In others the variations were within one plus or minus scale division of the Schiøtz tonometer. However, there is probably no mydriatic which may not precipitate acute glaucoma in cases that are predisposed to it.[3] As a measure of safety it should be followed by the administration of pilocarpine. In almost all cases the pupil returned to its original size within 90 minutes following the instillation of pilocarpine (1.0 to 2.0 percent).

Cyclomydril has a minimal cycloplegic effect. Any disturbance in vision noted was similar to that found with the use of any other strong mydriatic.

SUMMARY

1. Five years' experience with Cyclomydril has shown it to be a useful mydriatic of fast and effective action.

2. No rise in intraocular pressure or other undesirable effects were encountered.

3. It has minimal cycloplegic action.

4. Uneventful recovery of original pupil size within 90 minutes, in almost all cases, was achieved with the use of miotics.

57 West 57th Street (19).

315 Whitney Avenue (11).

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UNILATERAL EXOPHTHALMOS*

CAUSED BY METASTATIC CARCINOMA

RICHARD D. RICHARDS, M.D.
Iowa City, Iowa

Adenocarcinoma of the rectum is one of the more common types of carcinoma and is known to metastasis to unusual sites. However, I could find only one instance of metastasis to the orbit which had been reported in the literature.[1] A case of single metastasis to the orbit becoming evident more than five years after apparently complete removal of the original adenocarcinoma of the rectum without evidence of other metastasis or recurrence at the original site is presented.

* From the Department of Ophthalmology, College of Medicine State University of Iowa.

Fig. 1 (Richards). Front view, showing proptosis and depression of the right eye and the protuberance over the lateral wall of the orbit.

Fig. 2 (Richards). Sutures indicate area from which biopsy was taken.

Report of a case

A 71-year-old white retired farmer was first seen on February 27, 1959, because of progressive exophthalmos on the right side (figs. 1 and 2). The exophthalmos was first noted in December, 1958. Diplopia had been present for 10 days prior to admission. The only other complaints were mild episodes of pain over the right temporal area, poor appetite with weight loss of 10 pounds over a two-month period, and periodic episodes of abdominal pain.

Past history revealed that the patient had had an adenocarcinoma of the rectum which was apparently completely removed by means of a combined abdomino-perineal resection on November 9, 1953. At the time of operation, the lesion was found at 10 cm. on the posterior wall of the rectum and involved all layers of the wall. No lymph node involvement was found. Subsequent examinations did

Fig. 3 (Richards). A roentgenogram of the orbits shows loss of the linea innominata on the right. The posterior portion of the right orbit has a moth-eaten appearance, with loss of the superior orbital fissure, indicating bony involvement.

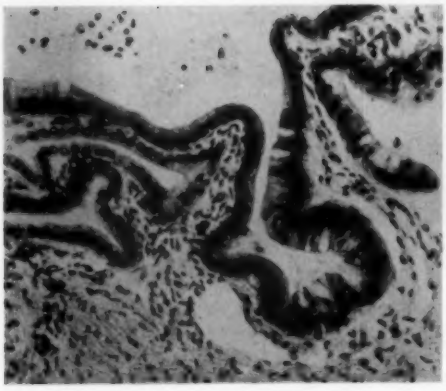

Fig. 4 (Richards). Microscopic section of the biopsy of the metastatic lesion in the right orbit, showing a well-differentiated adenocarcinoma of the rectum.

not reveal any evidence of recurrence or metastasis over a five-year follow-up period.

Ocular examination on February 27, 1959, revealed proptosis and depression of the right globe, and a nontender mass over the right temporal region. There was marked limitation of motion of the right globe in all directions. Vision was 20/80 and could not be improved. Fundus examination was normal except for pallor of the disc. Intraocular pressure was normal. Exophthalmometer reading was 15 mm. on the right and 9.0 mm. on the left (Luedde) The left eye was completely normal with vision 20/20.

X-ray films of the right orbit showed erosion of the wall posterolaterally involving the zygomaticofrontal process with extension into the sphenoid bone, and beginning erosion of the optic foramen (fig. 3). Left orbit, skull, and chest films were normal.

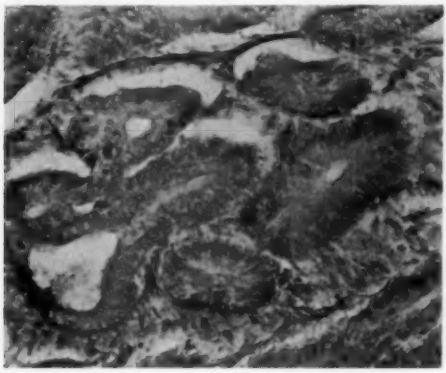

Fig. 5 (Richards). Microscopic section of the primary adenocarcinoma of the rectum.

A complete physical examination showed no evidence of recurrence of the original lesion or other metastasis. Positive findings were a moderate hypertension and evidence of an old anteroseptal myocardial infarct, and a moderately stenosed colostomy which caused intermittent partial obstruction and thus accounted for the abdominal pain.

A biopsy of the mass over the right temporal area was done (figs. 1 and 2). Immediately under the temporalis muscle a whitish, glistening, mucinous tumor was found. This tissue was extremely friable and had to be scooped out. Microscopic examination revealed a well-differentiated adenocarcinoma (fig. 4). A slide of the primary tumor removed more than five years previously was obtained and compared with the biopsy (fig. 5). The tumors are very similar, with the metastatic lesion being a little better differentiated than the original tumor.

Discussion

Although carcinoma of the rectum is one of the more common types of carcinoma and often metastasizes to unusual sites, I was able to find only one case in the literature with a metastasis to the orbit. Moore, in 1938, reported having had a patient with a carcinoma of the rectum which metastasized to the orbit, but no details were given.[1]

The only other case involving the lower gastrointestinal tract was reported by Forrest in 1949, in a review of orbital tumors.[2] In his case, a metastatic tumor was found in the orbit, and the characteristic microscopic appearance led to the discovery of the primary lesion in the colon. The portion of the colon involved was not stated.

The present case is unusual because of the site of the primary lesion, but even more remarkable is the length of time (over five years) that elapsed between removal of the primary and the onset of exophthalmos caused by the metastasis. The metastatic lesion is well differentiated, and the microscopic examination of the biopsy confirms the relationship to the primary tumor.

Summary

A case of unilateral exophthalmos caused by metastasis from an adenocarcinoma of the rectum is presented. The primary tumor

was removed more than five years before the exophthalmos caused by a metastasis was first evident, but no evidence of recurrence of the primary lesion or other metastases were found. Comparison of the microscopic sections of the primary and metastatic lesion confirm the common origin.

University Hospitals.

Dr. W. P. Standard, Macomb, Illinois, removed the original tumor and very kindly supplied an operative description and microscopic sections. Dr. F. C. Blodi, Iowa City, Iowa, assisted in interpretation and comparison of the microscopic sections.

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BLOW-OUT FRACTURE OF THE ORBIT*

W. L. Erdbrink, Cmdr. (MC) U.S.N.
Oakland, California

Orbital fractures occur rather commonly[1] but in a blow-out fracture, the orbital rim remains intact. With a blow-out or internal orbital type of fracture involving the floor of the orbit, there is a herniation of the orbital contents into the antrum. A restriction of elevation as well as depression of the globe results, producing diplopia, narrowing of the palpebral fissure, and an enophthalmos. With this herniation of the orbital contents, there is an incarceration of the inferior rectus and the inferior oblique muscles and the surrounding tissues into the fracture fragments of the orbital floor.[2] Immediate surgical correction of the deformity is urged by most authors.[3,4] The following case is of interest because, 15 years after injury, the diplopia was present on upward and downward gaze, but was absent in the horizontal positions of gaze where fusion was present.

Case report

A 24-year-old Caucasian seaman was admitted to the U. S. Naval Hospital, Oakland, California, March 23, 1959, with a chief complaint of "double vision." The past history revealed that at the age of nine years, while playing football, he "tackled" a man and was unconscious for about 12 hours. He remembered bleeding from the nose but denied the presence of a black eye. After regaining consciousness, double vision was present at all times. Approximately eight weeks after injury, the double vision was present only in looking up and down.

The vision was 20/20 in each eye. The left palpebral fissure was one mm. narrower than the right, and there was a two-mm. left enophthalmos.

* From the Ophthalmology Branch, EENT Service, U. S. Naval Hospital, Oakland. The opinions or assertions contained herein are those of the writer and are not to be construed as official or as necessarily reflecting the views of the Navy Department or of the Naval Service at large.

Fig. 1 (Erdbrink). Limitation of elevation and depression of the left globe.

Fig. 2 (Erdbrink). Waters' X-ray view, showing depression of the floor of the left orbit.

Red lens test showed diplopia in all of the cardinal positions of gaze except in the primary position and on levoversion and dextroversion. A right hypertropia was present looking up and right and up and left, the latter being greater. A left hypertropia was present down and right and down and left, the latter being greater (fig. 1).

Neurologic examination and an electroencephalogram were normal. Skull X-ray films were reported as being normal, as were stereo-Waters' X-ray views of the orbit (fig. 2). The patient and the X-ray films of the orbit were examined with Dr. Arthur Jampolsky, assistant professor of ophthalmology, Stanford University School of Medicine, who concurred in the impression of an old fractured floor of the left orbit, producing mechanical limitation of elevation and depression of the left globe with diplopia. No treatment was recommended since in the primary position diplopia was absent.

Comment

Better than eight percent of patients with zygomatic fractures complain of diplopia.[5] In the blow-out fracture of the orbit, this is a very common complication. Stereoscopic Waters' X-ray view of the orbit are indispensible in evaluating the case and laminography may be required to demonstrate this fracture. However, the restriction of elevation and depression of the globe should suggest a blow-out fracture when the orbital rim is intact.

In the blow-out type of fracture of the floor of the orbit, immediate surgical intervention, by elevating the orbital contents with a bone graft to the floor of the orbit, is mandatory before fibrosis takes place. This surgical management would obviate the persistence of diplopia which is an annoying physical disability and a serious cosmetic defect.[6,7]

Summary

A case of an untreated blow-out fracture of the orbit is presented. Fifteen years after injury, the patient had diplopia on upward and downward gaze due to limitation of movement of the left globe, but had the ability to fuse in the primary position.

U.S. Naval Hospital (14).

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GEOGRAPHIC DISTRIBUTION OF SENILE CATARACT

ADALBERT FUCHS, M.D.
Meran, Italy

Duke-Elder[1] gives two estimates of the incidence of lens changes in the various age-groups, one taken from Scandinavia and the other from America:

Age (yr.)	Anderson[2] (%)	Gradle[3] (%)
41-50	38.2	34.1
51-60	65.1	66.2
61-70	85.	68.4
70 +	92.	90.9

These statistics were not given as geographic information but to shed light on the different incidences of beginning senile cataract in the different age groups. From these data we learn that after 60 years more people have lens changes in Northern Europe than in the United States.

To get information about the frequency of senile cataract I sent out 1,028 questionnaires to eye hospitals and eye departments asking for the number of cataract operations; 367 questionnaires (35.6 percent) were returned.

Unfortunately it is not possible to compile reliable statistics on cataract operations because the number of the new patients in a year varies too much and thus we have no basis for comparison. Some hospitals have noted the number of in-patients, some all the patients who had come for treatment, not only new ones but also patients who had received treatment in former years. Table 1 shows the relation of new patients and cataract operations in a few hospitals.

One reason for the difference in the figures from various hospitals may be that now doctors of some of the insurance companies do not send their patients to eye hospitals or university clinics. That was certainly not so 30 years ago. To point up the frequency of cataract Table 2 lists the statistics of H. H. Chang,[11] based mostly on very old publications.

Table 2 shows amazingly high figures for France and Manila. France showed 14 percent. My statistics on four hospitals with 24,932 new patients showed 334 cataracts, 1.33 percent. Manila noted 14.78 percent, while I found in four hospitals with 21,465 new patients 408 cataracts, 1.62 percent. I do not think that the cataracts were more frequent in former days; probably cataracts are now operated on in more places than formerly.

Studying the frequency of cataract I believe it does not vary very much in America, Europe, Australia, and Asia with two noteworthy exceptions, which I will discuss later.

In 1933[4] I pointed out that cataract is by no means common on the high plains of the tropical states of west South America, certainly not more common than in Europe. One would expect more cataracts there, as the light at 12,000 feet altitude is dazzling and the ultraviolet rays very powerful. Some doctors thought that the strong impact of light is the cause for frequent high myopia while other scientists denied that high myopia is frequent in the higher parts of Bolivia. Unfortunately questionnaires from Latin America are not numerous. Only two hospitals in Santiago, Chile, reported 2.3 percent cataract operations in new patients in a year and four hospitals in Brazil show 4.4 percent.

The reports from Africa were few. Dr. Watters, Ganta, Liberia, wrote: "We see a high number of cataracts but I have no figures on that. We see quite a number of cases where native practitioners 'treated' cataract patients by dislocating the lenses back into the vitreous causing temporary vision, then inflammation and finally complete blindness." Dr. Sigmund, Basutoland, informed me that he has seen among 5,511 patients 23 senile cataracts (0.41 percent). According to Vanneste[5] senile cataract is very frequent among Negroes in the Congo due to premature aging.

It is amazing that cataract is very frequent in special areas in India and Pakistan. In certain districts[6] senile cataract is so fre-

TABLE 1

RELATION OF THE NUMBER OF NEW PATIENTS IN A YEAR TO CATARACT EXTRACTIONS

Place	Patients	Extractions	Percent
New York City	88	43	43.4
Bronx, New York	5,794	360	6.2
Boston	5,845	79	1.3
Würzburg, Germany	8,337	149	1.7
Berlin, Germany	4,320	145	3.3
Göttingen, Germany	4,612	72	1.5
Rome	17,380	326	1.8
Quetta, Pakistan	7,600	1,965	25.8
Bhiwani, Punjab-India	45,716	7,596	16.6
Bombay	27,137	1,373	5.0
Madras	59,682	2,471	4.1
Colombo, Ceylon	70,479	1,523	2.16
Tokyo	6,272	92	1.4
Tokyo	4,576	143	3.1
Aomoriken, Japan	2,500	35	1.4
Kobe, Japan	5,009	226	4.5
Melbourne	30,280	216	0.71
Sidney	2,180	123	5.6

quent that some surgeons operate on several thousand cases a year, often nearly 100 a day. A special method of operation was invented to enable them to cope with so many operations and the postoperative treatment. The cataract is not only much more frequent than in our countries but develops at a much earlier age so that people at the end of their forties, as a rule in the fifties, are operated on for senile cataract. It was maintained that this early beginning of cataract is due to a special early senescence. I can hardly believe that, first, because life expectancy in India does not seem so much shorter than it was in olden times in Europe and, second, because other signs point to a special vitality of the people in old age. For instance, in Ceylon I removed a cataract from a Singhalese aged 86 years and when he was dismissed from the hospital, he asked me, immediately, if he could take up sexual intercourse with his wife again!

Rambo,[7] Vellore, N.A., India, writes: "A practical survey of the Central Provinces (Madhya Pradesh) indicated that one of every hundred of the population had operable cataract."

That senile cataract is very frequent in India is also proved by the fact that, like Elliot, Caccamise[8] found 30 percent of the cataract patients had a morgagnian cataract —apparently many cataract patients do not go to a surgeon in time. Wright, who for many years worked in Madras, wrote me: "I imagine the frequency is much the same taking the Indian peninsula as a whole."

It seemed possible that the large incidence of cataract in this enormously populated land is due to the small number of eye doctors (0.0012 per mille). But this idea was not accepted by my friends and colleagues in India (Wright, Holland and Banaji).

Dr. S. N. Cooper from Bombay wrote:

> The incidence of cataract is equal in the two sexes on the whole. One ophthalmic surgeon draws attention to the incidence of a state of dehydration in some of his cataractous cases. Another surgeon feels that a high incidence of cataract was found in the Sindhi community when the Sindhis evacuated from the province of Sind (Pakistan) into India as

TABLE 2

FREQUENCY OF CATARACT (CHANG[11])

Author	City	Number of New Patients	Percentage Cataract Operations
Arlt	Vienna (Austria)	8,451	5.10
Becker	Heidelberg (Germany)	11,872	3.70
Knapp	Heidelberg (Germany)	10,498	5.70
Knapp	New York (U.S.A.)	6,379	2.80
Pagenstecher	Wiesbaden (Germany)	14,619	6.30
Steffen	Frankfurt (Germany)	44,210	3.00
von Wecker	Paris (France)	13,290	14.00
Horner	Zürich (Switzerland)	5,000	3.60
Ubald a.Ayuyao	Manila (Philippines)	3,748	14.78
Thacker-Neville	Mukden (China)	2,287	1.74
Pi, H.T.	Peiping (China)	12,111	0.65
Chang, H. H.	Chengtu (China)	2,789	2.61

refugees. He believes that this may be due to a great mental strain and lack of nutrition. Another surgeon of Delhi believes that it is due to malnutrition, ill-balanced diet and deficient vitamins, but does not give any reason for this assumption.

Dr. Mathradas Pahwa who has done perhaps the largest number of cataract operations in the world, about 200,000, believes that the incidence is highest in Kashmir and in the Uttar Pradesh, that is in the valley of the Ganges and the Jumna rivers. The incidence is also very high in Punjab and Sind and the provinces irrigated by the Indus and its five tributaries. The incidence is perhaps lower in Rajputana (now Rajasthan) which is comparatively a barren area. But the population of Rajasthan is less per sq. mile than that of Uttar Pradesh.

Dr. Tajkeff, a Polish ophthalmologist practising in Calcutta, believes that there is no higher incidence of cataract in India than elsewhere, as well as he can judge from his private practice. He feels that his foreign colleagues who occasionally visit India may be so impressed by the great number of cataract operations they see in the hospitals that they are likely to forget the size of the Indian population, and the relatively restricted number of hospitals in which all the cases are concentrated.

I feel that the incidence of cataract, though higher in India than elsewhere in the world, is almost evenly distributed in the whole of the country, not sparing any race or sex. I have very little experience with cataracts in the European population because it is a floating population and probably they leave the country by the time the cataractous age creeps on them. In Dr. Mathrades' impressions about uneven distribution there is a fallacy. The province of Uttar Pradesh is along the Ganges and Jumna, and Punjab and Sind are along the Indus river. These are the most thickly populated provinces of India, whereas Rajasthan is a desert, and mainly the population is on the sides of the Aravali hills and above the Nerbada river and the Vindhya mountains. My impression is that there is no preponderance of cataract in any particular part of India.

TABLE 3

RELATION OF NEW PATIENTS A YEAR TO CATARACT EXTRACTIONS IN PAKISTAN AND INDIA

Place	Patients	Extractions	Percent
Quetta	7,600	1,965	25.8
Bhiwani	45,716	7,596	16.6
Amritsar	24,246	1,896	7.8
Delhi	26,924	955	3.5
Delhi	2,728	13	0.47
Luknow	16,235	466	2.8
Sitapur	37,059	3,740	10.1
Jaipur	14,157	680	4.8
Vrindaban Mathura	14,041	406	2.9
Bamdah, Bihar	23,936	2,001	50.8
Bombay	27,137	1,373	5.05
Bombay	16,013	519	3.2
Bombay	18,505	955	5.1
Calcutta	64,163	2,209	3.4
Ratlam, Madya Bharat	8,000	200	2.5
Indore	18,306	914	5.0
Madras	59,682	2,471	4.1
Bangalore	46,773	927	1.9
Coimbatore	22,000	1,300	6.0
Assam	4,404	130	2.9

I have tried to ascertain the incidence of cataract by a comparison of its incidence against glaucoma and the total attendance in the department which, however, cannot be considered scientifically correct. In any case it will be more correct than trying to compare the same with the total population of the state. In the latter instance there are such a number of patients who cannot visit the hospital, and places where hospital facilities are very poor. I believe that the incidence of cataract operations and glaucoma operations against the total attendance in the eye department of a hospital will at least give us a percentage of the cataracts and glaucomas which can be used for comparison with similar percentages over the world.

The figures for the last three years are as follows:

Year	Total In-Patients	Total Glaucoma Operations	Total Cataract Operations
1955-1956	907	76	520
1954-1955	929	60	547
1953-1954	988	62	595

I may also draw your attention to the high incidence of black cataracts and lens sclerosis in our country, which is the cause of one variety of myopia. I wonder whether lens sclerosis with browning of the posterior cortex is quite as common in non-Indian countries.

My best information on the regional distribution of cataract came from Mr. R. W. B. Holland, the son of Sir Henry Holland, who had worked for many years in Quetta, Pakistan. He wrote me:

All along the Indus valley and that of its tributaries, and in Bihar Province, cataract is known to be very frequent. Old people expect to get cataract. My father, Sir Henry Holland, who himself has been responsible for the removal of 50,000 to 80,000 cataracts, has developed this in both eyes, my mother, who was also there for about 50 years, has done so too. One old hospital nurse, after 39 years service, has also developed it. So it would seem, possibly, to be an acquired phenomenon to some extent. Possibly the drought (rainfall three to eight inches, yearly) and strong ultraviolet light might have some influence.

Cataracts are as frequent in sparsely populated areas as in the densely populated ones. The proportion I do not know.

I do not think there is any racial cause at all.

I don't see how the scarcity of eye doctors can influence the number of cataracts.

The percentage of diabetic cataract is very small —0.001 percent (about) of all cataracts.

When the findings culled from the 360 questionnaires are compared with this letter from Mr. Holland, all of his statements are verified (table 3).

Quetta (Pakistan), 25.8 percent, Bhiwani (Punjab), 16.6 percent, Bamdha (Bihar), 50.8 percent show the greatest number of cataract extractions. The other percentages are about the same as those for the United States, Europe, and Australia. The only larger percentage (10.1 percent) is noted in Sitapur, another city of U.P. However, Luknow, lying south of it, show only 2.8 percent.

It is interesting to hear that both parents of Mr. Holland and a nurse got binocular cataract. Apparently that shows a local cause. Since the same strong ultraviolet light and drought are present in so many parts of the world, in Northwest China, Africa and America without a high number of cataract, I am inclined to believe that some special factors are inherent in the soil or in the food.

We see that different ophthalmologists working in India, differ very much in their opinion but we may still assume that senile cataract is much more frequent in some Indian territories than in others. As we do not know very much about the origin of senile cataract, a better knowledge of those parts of India where senile cataract is especially frequent may lead us to new investigations and a new knowledge of some etiologic factors.

Cataract is rare in China. Maxwell[9] considered cataract "not a specially common disease in China."

According to my[10] inquiries in 1924:

Senile cataract seems to be less frequent all over China than in Europe. The same holds good for Manchuria where in the hospital in Mukden 3,000 patients were treated in a year and 16 cataracts (0.53 percent) were operated on. In Korea the number of cataracts is seemingly more frequent than in China and in Japan the amount of cataract is more or less the same as in Europe, possibly somewhat larger; as Prof. Ichikawa in Kyoto operated about 200 cataracts among 6,000 new patients in a year (3.3 percent).

It is striking that one encounters only very rarely old people with white hair on the roads of China while in Korea one can see many. Possibly one reason is that the hair of the Chinese begins to turn gray much later than that of Europeans and it is very frequent that one sees people of 60 or more years, even 65, who have quite dark hair. The people in Japan, as I was told, do not get as old as Europeans; this may be caused by the not very nutritious food they get. Ripe senile cataract is mostly observed between 55-60 years. That means much earlier than in Europe.

It is quite difficult to guess the frequency of cataract in China because without doubt many Chinese do not care if their vision decreases with advancing age or if they get blind. Old people no longer work as their children have to take care of them according to the law. They hardly ever leave their houses as nature in many parts of China is not very attractive during many months of the year and the wind and dust keep them in their homes where they can orient themselves quite well. Old people also read only exceptionally; frequently their children and grandchildren do their reading for them. Dr. Grimm, a German ophthalmologist in Tsinanfu had operated on seven patients with cataract very successfully and promised to give them cataract-glasses gratuitously later on. Not a single one of these patients returned to get glasses although they lived in the same city. They were all satisfied with the amount of vision they got by the operation and were not eager to improve it.

Specially important I consider the fact that I so rarely saw incipient cataract, which shows a small frequency of cataract in China.

The statistics of H. T. Pi in Chang's[11] paper of 0.65 percent prove my statement.[10] Later W. S. Mao[12] found senile cataract in 2.51 percent of all eye cases.

There is a discrepancy concerning cataract operations in Japan: Prof. Ichikawa told me in 1925 that he had operated on 3.3 percent of his new patients, while now two hospitals from Kyoto show 1.7 percent (125 extractions in 9,515 patients). In general, according to the questionnaires, the frequency of cataract in Japan is similar to that in Europe.

According to Dr. Cooper diabetes is very frequent in India due to carbohydrates (rice) being the staple diet of the majority of the population, but does not appear to contribute more than three percent to the incidence of cataract. The highest incidence of diabetes in cataractous patients has been reported from

New Delhi's Dr. Schroff's Charity Eye Hospital, about six percent.

Diabetic cataract in Quetta was estimated by Mr. Holland as about 0.01 percent. In China Chang[11] found a very small number of cases, 0.8 percent. I had the impression that in South India and Ceylon diabetic cataract is much more frequent than in Vienna.

It would be a great service if the International Council of Ophthalmology would consider an "ophthalmologic year" similar to the "geophysical year." The main object would be to compose an adequate, precise questionnaire and to send it out to all the eye hospitals and eye department in the world; they would be asked to collaborate and make exact statistics for one year. Such research would bring an immense advantage to our specialty.

Karl Wolfstrasse 14.

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Ophthalmic Miniature

I determined to puncture the (detached) retina in hope of improving sight. At evening, with the aid of Dr. Agnew, who held the upper lid, I performed the operation. The patient, placed under a gas light, and the eye illuminated by a mirror attached by an elastic band to my forehead, a broad, double-edged needle was entered between the superior and external recti muscles, and advanced until its point was distinctly seen in the vitreous humor; it then was plunged into the highest part of the retinal sac, and the point carried backwards to enlarge the perforation. Blood at once flowed into the vitreous. Applied a compress and bandage.

H. D. Noyes,
Cases, of Sub-Retinal Effusion,
Tr. Am. Ophth. Soc., **1**:part 2;36, 1866.

OPHTHALMIC RESEARCH

EDITED BY FRANK W. NEWELL, M.D.
950 East 59th Street, Chicago 37, Illinois

Abstracts of papers presented at the meeting of the East-Central Section of the Association for Research in Ophthalmology, Inc., Rackham Amphitheatre, Ann Arbor, Michigan, January 4, 1960.

V. Everett Kinsey, *Section Secretary*
Kresge Eye Institute, Detroit, Michigan

Parasympathomimetic properties of ocular extracts. Morton B. Waitzman, Ph.D., Laboratory for Research in Ophthalmology, Western Reserve University, Cleveland, Ohio.

Parasympathomimetic properties of substances extracted from hog ocular tissues have been investigated. Assay procedures were performed on muscle bath preparations of rat colon. Ambache (J. Physiol., **135**:114, 1957) described such properties for similar extracts of rabbit irises.

It was found that parasympathomimetic effects, not acetylcholinelike (contractions not affected by atropine), were present in extracts of ciliary muscle, iris dilator pupillae, and whole iris tissue. Parasympathomimetic effects which were acetylcholinelike (effects reversed by atropine) were present in ciliary process extracts. These results may have implications concerning any effects these substances might have on the accommodation, or pupillary reflexes, or on some phases of aqueous humor dynamics.

A method for evaluating local anesthetics in ophthalmology: A preliminary report. William G. Everett, M.D., and James W. Finlay, M.D. Department of Ophthalmology, University of Pittsburgh, School of Medicine, Pittsburgh.

Anesthetic blocking agents utilized in ophthalmic surgery have been studied by comparing abolition of sensation or pupillary reflex. The duration of the motor block resulting from injection of these drugs has not been considered. A new method of evaluation of drug-induced oculomotor paralysis by employing the phenomena of optokinetic nystagmus in monkeys is presented.

Tonometry as a research tool. Elizabeth P. Olmsted, M.D., Buffalo, New York.

The indentation tonometer of Schiøtz possesses an intrinsic error in its susceptibility to variations in "scleral rigidity" from eye to eye. However, due to its high utility in the measurement of intraocular fluid dynamics, methods have been developed to correct this error by combining indentation and applanation tonometry directly to measure the scleral rigidity coefficient of the individual eye. It is suggested that this measurement is of itself useful as a criterion of scleral tissue elasticity in the study and evaluation of a variety of physical conditions manifested in the eye.

The lowered scleral rigidity recorded in myopia is cited as a manner of studying the altered refractive state of the eye. Evidence of reduced scleral tone in thyrotropic exophthalmos as contrasted to an increase in thyrotoxic proptosis is offered as a means of furthering understanding of endocrine exophthalmos. This is interrelated with recent indication of change in scleral rigidity with water metabolism, giving a further point of contact of scleral tone to endocrine function.

Structural details of the emissaria of the canal of Schlemm. H. R. Hausler, M.D., and Th. M. Sibay, M.D., University of Toronto, Toronto, Ontario.

The canal of Schlemm was injected in 10 human eyes with the aid of a microcannula and using a silver staining technique. It was found that the silver solution was carried through the emissaries of the canal to the subconjunctival venus plexus, and that the emissaries had characteristic structural details, as shown on a number of slides.

Some structural details observed on retinal blood vessels of diabetic patients. H. R. Hausler, M.D., and Th. Sibay M.D., University of Toronto, Toronto, Ontario.

Five post-mortem eyes of five patients with diabetes mellitus were injected through the central retinal vessels using a silver staining technique. The retinas were viewed as cleared flat preparations and it was possible on these preparations to study the whole vascular tree in its continuity and also observe structural details of individual vessels. All retinas showed multiple microaneurysms but retinitis proliferans was only demonstrated in one specimen in the form of several rete mirabiles growing forward into the vitreous. The outline of capillary endothelial cells was found absent in the dilated parts of the capillary forming the aneurysm—if the aneurysm was of the type showing dilatation of only one side of the capillary wall, the endothelium was usually preserved in the undilated portion. A peculiar brown-yellowish staining area was seen lining most of the arterioles. This was never observed in preparations of normal retinas.

Drainage openings in the trabecular wall of Schlemm's canal. J. S. Speakman, M.D., Toronto, Ontario.

A previous study of the inner wall of Schlemm's canal, using flat teased preparations and thin paraffin sections, disclosed large openings and deep grooves. In addition an unusual degree of vacuolation was seen in the endothelial cells lining the canal which was attributed to post-mortem degeneration.

A further examination of this region has been made in both monkey and human eyes, employing rapid fixation techniques to rule out post-mortem artefact in order to interpret the significance of the endothelial cell morphology more accurately. New evidence suggests that the structures which were previously thought to be vacuoles are in fact the openings of numerous small channels through which aqueous can enter Schlemm's canal from the trabecular meshwork.

Some structural details of the canal of Schlemm and its emissaria. H. R. Hausler, M.D., and Th. Sibay M.D., University of Toronto, Toronto, Ontario.

The canal of Schlemm was injected in 10 normal post-mortem human eyes, using a silver staining technique described earlier. It was found that the silver solution was carried through the canal to the episcleral and conjunctival venous plexus, producing characteristic staining of the endothelial cell boundaries. The preparations were studied after they had been cleared in glycerine.

The scleral wall of the canal itself was found to be lined by an endothelium of elongated spindle-shaped cells with their long axis mostly parallel to the axis of the canal. This pattern is interrupted around the openings of emissary vessels, where the endothelial cells assume a more irregular shape. The endothelium of the trabecular wall of the canal also consists of spindle-shaped cells but the long axis of these cells frequently lies at an oblique or right angle to the axis of the canal and, occasionally, the cells are arranged in whorl-like patterns.

The emissary vessels of the canal mostly divide up immediately into a dense intrascleral plexus, where many complete vascular circles are formed. The irregularity in the shape and caliber of these vessels is striking. They are lined by endothelial cells which are wider and not as elongated as those lining the canal. A few emissary vessels show a fairly straight course through the sclera to the episcleral and conjunctival plexus. These vessels might form what is clinically seen as aqueous veins.

Ultrastructure of the human iris. Abbott T. Kissen, Ph.D., Department of Ophthalmology, The Ohio State University, Columbus, Ohio.

Iris tissue obtained at cataract surgery was prepared for electron microscopy study in the following manner. The tissues were fixed in osmium tetroxide, dehydrated in the alcohol series and divided into two groups for embedding. One group was embedded in the standard n-butyl methacrylate medium, the other in an epoxy resin, Araladite. The purpose of the segregation was to compare the ease of preparation and the quantities of resolution.

The pigment epithelium was studied and described. An extension of the posterior chamber as an intercellular fissure is also noted and its possible significance is discussed. Cytoplasmic/cytomembrane elaborations of the pigment epithelial cells are described. The transition zones between the pigment epithelium and underlying muscle cells were studied and the presence of a basement membrane separating the two layers of tissue was observed and described. Three types of stromal chromatophores, designated as A, B, and C were noted. The classification of the stromal cells is based upon the morphology of the nucleus, the amount and distribution of pigment granules and cytoplasm. As for the embedding material, it was concluded that Araladite is equal, if not superior, to methacrylate.

An investigation of the effect of autonomic drugs on the iris. Donald R. Bennett, M.D., Robert D. Biggs, M.D., and Mathew Alpern, Ph.D. Departments of Pharmacology and Ophthalmology, University of Michigan Medical School, Ann Arbor, Michigan.

The iris muscles are useful test objects for autonomic drug-receptor studies. However, parenteral administration of drugs produces both direct and centrally mediated reflex effects on one or both muscles. Conversely, isolated iris preparations have the usual disadvantage of such methods. In order to obviate some of these problems, drugs have been injected into the posterior chamber of the eye. Unanesthetized rabbits are employed. With a few modifications, the guinea pig may also be utilized. Pupil size is determined with a camera. Volume of fluid injected is limited to 0.05 ml. through a No. 30 gauge needle. Drugs are diluted in normal saline. Injection of 0.05 ml. saline produces little alteration of pupil size compared to normal alteration of pupil size in uninjected control eyes. A marked mydriasis, persisting for approximately 90 minutes, is produced by 2.0 mg. of l-epinephrine HCl. Dose response relationships for the d and l isomers of epinephrine, norepinephrine, and isoproterenol have been determined and will be presented. Data on the effectiveness of parentally administered dibenzyline and dichloroisoproterenol to prevent the responses of the above adrenergic drugs will also be presented.

The role of fructose in lens metabolism. John F. R. Kuck, Jr., Kresge Eye Institute, Detroit, Michigan.

Fructose is relatively inactive in lens metabolism. The lens uses glucose preferentially over fructose and if no glucose is available the utiliza-

tion of fructose is but a fraction of the normal glucose utilization. Furthermore, the lens capsule is less permeable to fructose than to glucose. The fructose in the lens is apparently merely the by-product of a system whose primary function is the recycling of phosphopyridine nucleotides. Glucose is reduced to sorbitol with the concurrent re-oxidation of TPNH produced by the hexosemonophosphate shunt. Sorbitol is then oxidized to fructose with the concurrent reduction of DPN produced by glycolysis.

Composition of the vitreous humor in relation to that of plasma and aqueous humor. D. V. N. Reddy, Ph.D., and V. Everett Kinsey, Ph.D., Kresge Eye Institute, Detroit, Michigan.

The chemical composition of the vitreous humor in relation to that of the aqueous humors and plasma of the same rabbits has been determined.

The concentration of sodium in the vitreous was found to be lower than that in the other intraocular fluids and the plasma. The deficiency of this cation was balanced approximately by an excess of potassium. The concentrations of chloride, bicarbonate, and ascorbate in the vitreous were found to be intermediate between that of the plasma and the posterior aqueous humor. The concentration of lactate in the vitreous was indistinguishable from that of the aqueous humors or plasma, and that of phosphate, glucose, and nonprotein nitrogen was slightly lower than that of these fluids.

The implication of these findings in relation to the intraocular fluid dynamics of the aqueous of the posterior chamber is discussed.

The macrophages of the human retina and vitreous. J. Reimer Wolter, M.D., Department of Ophthalmology, University of Michigan Medical School, Ann Arbor, Michigan.

Numerous stages of nonspecific reaction of the macrophages of the human retina and vitreous were studied with a special technique in many pathologic eyes. From the observed stages of rest, migration, phagocytosis, transport, delivery to the blood stream, accumulation, and degeneration of these cells it was possible to understand their nature and to gain an impressive view of their functions.

Clinical experiences with the light coagulator. William H. Havener, M.D., Department of Ophthalmology, The Ohio State University, Columbus, Ohio.

The known indications for light coagulation are actual or incipient tears without extensive detachment, treatment supplementary to standard detachment surgery, some intraocular neoplasms and some iridectomies. The indications are still being evaluated in inflammations. Possible detrimental effects are discussed.

Light scatter within the frog retina. Leo E. Lipetz, Ph.D., Department of Ophthalmology and Institute for Research in Vision, The Ohio State University, Columbus, Ohio.

Measurements made on living, isolated frog retinas showed that they scattered light as a function of angle and wavelength in much the same manner as ground glass. The intensity of light doubly scattered within the retina so that it emerged from the back side perpendicular to the retina was measured as a function of the distance from the edge of the incident light beam. The functions so determined for the unbleached and bleached retinas are compared with the spatial summation functions for the frog and human retinas as deduced from other work.

The use of domestic animals for experimental ophthalmology. Jack H. Prince, Institute for Research in Vision, Ohio State University Research Center, The Ohio State University, Columbus, Ohio.

There is a growing awareness that the ocular anatomy of the animals used in experimental ophthalomology is sufficiently different from that of man to make the results of some experiments quite inadequate as a basis for application to human subjects or patients. It is also becoming evident as a result of our extensive anatomic dissections that there may be animals which have hitherto been ignored, but which are easily available for special types of experiments.

An hypothesis concerning the etiology of strabismus in nonparalytic strabismus. Samuel C. McLaughlin, Jr., M.S., Department of Ophthalmology, University of Michigan, Ann Arbor, Michigan.

An hypothesis is advanced concerning the etiology of strabismus in patients who have no sensory or motor obstacle to fusion. The hypothesis assumes that the cause of onset in these patients is a temporary or remediable condition which is no longer present at the time of examination, and that the persistence of the strabismus is to be accounted for in terms of a perceptual disorder which is acquired in adaptation to the temporary condition. A specific perceptual disorder is described; it is shown that this disorder is present in all patients who have a well-established strabismic condition; and it is shown that the disorder constitutes an obstacle to fusion and is capable of accounting for the persistence of the strabismus condition.

An apparatus and procedure for use in the management of comitant strabismus. Samuel C. McLaughlin, Jr., M.S., Department of Ophthalmology, University of Michigan, Ann Arbor, Michigan.

A novel method of treating strabismus patients has been described previously. An apparatus and procedure which greatly facilitates the clinical application of that method is described. The apparatus consists primarily of a light box which, when used in conjunction with a suitable polaroid

viewer, presents a different configuration to each eye. The two configurations are independently illuminated, and can be turned on and off separately by means of switches which are operated by the examiner.

Changes in the pigment granule composition of the human retinal pigment epithelium during aging. Barbara Wiard Streeten, M.D., Department of Ophthalmology, University of Michigan Medical School, Ann Arbor, Michigan.

Of all the functions of the retinal pigment epithelial cell, that of pigment production is the most obvious, yet even the normal distribution of pigment has not been adequately described. A study of the pigment epithelium has been made in 25 normal human eyes, from fetal life through the age of 70 years. By the use of whole mounts and frozen sections, consistent changes in the regional granule population can be followed over this age span. Especially interesting is the appearance of almost colorless granules, apparently in the early postnatal period. While sparse at first, these granules become extremely numerous with morphologic differences regionally. Their intense sudanophilia with Sudan Black B and other related histochemical characteristics set them apart from the familiar cigar or spindle-form granules. Their relationship to the more pigmented round forms appears to be closer.

A modification of ophthalmodynamometry in occlusive disease of the carotid artery. Manos A. Petrohelos, M.D., and Richard E. Preston, M.D., University of Michigan Medical School, Ann Arbor, Michigan.

Recognizing the need for refinement of diagnostic procedures in detecting occlusive disease of the carotid artery a modification in the usual technique of ophthalmodynamometry was tried. Patients clinically suspected of having such a condition were placed on a "tilt-table" and retinal artery pressures were determined simultaneously with systemic blood pressure in each arm. The procedure was then repeated after tilting the subject into an upright position of either 45 or 80 degrees. All patients with established occlusion or severe insufficiency (the majority having angiographic confirmation) revealed an accentuation of the retinal artery pressure difference between the two eyes when tilted to the upright position.

It appears that tilting of the patient from supine to erect or semi-erect position affords a provocative means of sensitizing ophthalmodynamometry and thereby refining its already established use in carotid artery occlusive disease.

How valid is a scleral tonometer? Raymond E. Hogg, M.D., and Mathew Alpern, Ph.D., Department of Ophthalmology, University of Michigan Medical School, Ann Arbor, Michigan.

Wolfe has described a tonometer designed to measure the intraocular pressure when placed on the sclera. Experiments have already established that measurements with this type of instrument are quite repeatable. The present study was carried out to determine how accurately a scleral tonometer actually measures what it purports to measure. The study was divided into two parts:

In the first part, 11 enucleated animal eyes were subjected to various pressures which could be accurately measured with an open-tube water manometer and the intraocular pressure was determined simultaneously with the scleral tonometer. As a control the same measurements were also carried out with a standard clinical (Schiøtz) corneal tonometer. The scleral tonometer appeared to be much less sensitive to changes in pressure than the corneal tonometer and the results from the latter appeared to be less variable. On the average changing the intraocular pressure by 55.1 mm. Hg was associated with a measured difference of pressure of 51.2 mm. Hg with the corneal tonometer, but only 22.5 mm. Hg with the scleral tonometer. When the measured pressure was plotted against the induced pressure the slope of the average curve for the corneal tonometer was 0.91; for the scleral tonometer it was 0.41. When the results for the two instruments were compared on individual eyes, the corneal tonometer curves showed significantly greater slopes (p 0.001) than did the ones for the scleral tonometer.

In the second part measurements were made with the two instruments on 86 eyes of clinic patients. The results of the second part are in agreement with those of the first part—the scleral tonometer appeared to be much less sensitive than the corneal tonometer. Although the correlation coefficient between the two measurements ($r = 0.596$) is significantly larger than zero, it is not large enough to validate the use of this particular scleral tonometer as a method of measuring the intraocular pressure.

The frequency distribution of visual acuity among a group having 20/20 vision or better. Clement McCulloch, M.D., N. C. Turnour, F/L, J. R. Smiley, F/L, and A. W. Brown, F/O, Institute of Aviation Medicine, Toronto, Ontario.

Using a set of 41 slides, the visual acuity of personnel, having at least 20/20 visual acuity unaided, was determined. A group of 87 subjects had a mean visual acuity of 20/10 with a standard deviation of 1.34. The difference of the means for the 100 percent, 50 percent and zero pass levels was one acuity unit for each interval.

Visual functions of "typical" and "atypical" congenital achromatopsia.* H. Richard Blackwell, Ph.D., and O. Mortenson Blackwell, A.B., Institute for Research in Vision and Department

* Measurements made while we were associated with the Vision Research Laboratories and the Department of Ophthalmology, University of Michigan. The patients were examined and referred by Harold F. Falls, M.D.

of Ophthalmology, The Ohio State University, Columbus, Ohio.

The visual functions of 10 male congenital achromats and various members of their families have been subjected to extensive psychophysical study. Measurements include color discrimination, luminosity at two luminance levels, acuity as a function of luminance in white and blue light, dark adaptation for white and blue test stimuli at the fovea and at a 15-degree peripheral location. Three categories have been established into which eight of the cases can be fitted.

The first category corresponds to what has been called typical achromatopsia. These patients exhibit the typical rod photoreceptor system only.

The second category corresponds to what we have previously designated blue monocone monochromacy. These patients exhibit a monochromatic system at high luminance with a narrow action spectrum peaking at about 440 millimicrons. They exhibit a monochromatic system at low luminance with an action spectrum corresponding to the usual rod action spectrum, modified by 70-percent concentration of macular xanthrophyll. At intermediate luminance levels these patients exhibit a dichromatic system based upon blue cones and rods.

The third category is intermediate between the first two. At high luminance, there is a monochromatic system with an action spectrum representing a mixture of blue cones and rods. At low luminance there is a monochromatic system with the usual rod action spectrum.

The remaining two patients fitted into different categories under different conditions. For one, this was shown to depend upon the mode of fixation. These results suggest that many cases of typical and atypical achromatopsia may have equivalent sensory mechanisms.

Newer methods for eye research. J. M. B. Bloodworth, Jr., M.D., The Ohio State University, Columbus, Ohio.

This laboratory is engaged in the study of flat preparations of the retina and choroid from routine autopsy material. The major problem under study is diabetic retinopathy and a search for related vascular changes in the flat preparations of the choroid. The techniques involved are the flat preparation of the whole retina and choroid followed by re-imbedding of unusual areas with routine histologic sections and special stains.

Centrally fixed flicker thresholds in amblyopia. Mathew Alpern, Ph.D., Donald B. Flitman, M.D., and Robert H. Joseph, M.D., Department of Ophthalmology, University of Michigan Medical School, Ann Arbor, Michigan. (Assisted by Grant No. B-1578 from the United States Public Health Service, Department of Health, Education and Welfare.)

It has been variously reported that the critical flicker frequency for the center of the field in the amblyopic eye is lower than, and the same as, that of its nonamblyopic fellow. Either of these results is easy to obtain, depending on whether or not the fluctuations in the diameter of the pupil are prevented from influencing the amount of light reaching the retina. In order to find out whether this is due to the influence of light at a specific retinal illuminance, the relationship between critical flicker frequency and retinal illuminance was determined over a wide range in the normal and amblyopic eyes of a number of such observers. The results were analyzed in terms of current theories of the nature of the reduction of vision in amblyopia.

SOCIETY PROCEEDINGS

EDITED BY DONALD J. LYLE, M.D.

NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY

March 2, 1959

SHORTENING ANTERIOR CHAMBER IN ANGLE-CLOSURE GLAUCOMA

DR. GEORGE GORIN described a group of cases of glaucoma with an atypical mode of closure of the angle. Instead of the angle closing first at its entrance, as is the rule, a progressive closure, beginning in the periphery of the angle and progressing toward the line of Schwalbe, occurred, the closure consisting of a permanent fusion between the root of the iris and the trabeculae overlying the canal of Schlemm. This appears gonioscopically as "shortening of the angle."

Gonioscopically the classical acute angle-closure glaucoma shows a closed angle during an attack, and reopened angle between attacks. In the present type of case, the anterior part of the trabecular meshwork is visible even when tension is elevated. This may, therefore, appear to be an "open angle" when in fact it is closed. The differential diagnosis is whether the whole trabecular band, and particularly the scleral spur, can be seen. If it can be seen, shortening of the angle does not exist. If it cannot be seen, then either shortening exists or the angle is too narrow to permit visualization. These cases can sometimes be differentiated by examining the displacement of the focal lines of the slitbeam at the angle.

The cases presented had the following features:

1. Shortening of the angle due to synechias produced by an assumed pathologic process; the adhesions began posterior and advanced forward. In the late cases the iris is pulled up to the line of Schwalbe and the angle is completely closed.

2. The chamber is not shallow; it is normal or moderately deep.

3. A noncongestive course. Impairment of outflow sets in gradually and tension is only moderately elevated.

4. Dark-room test and mydriasis increase the tension.

Early iridectomy is the best treatment. Delay results in gradual progressive closure. Even after early iridectomy, miotics may be necessary since some of the synechias may have permanently blocked part of the trabecular meshwork.

Discussion. DR. ADOLPH POSNER: Dr. Gorin's paper is a distinct contribution to the management of glaucoma. The type of angle which he describes has always puzzled us and must have puzzled many others who look to gonioscopy for aid in the diagnosis and classification of glaucoma.

I examined gonioscopically the patient whose case Dr. Gorin reported and found the angle open when the tension was elevated, hence I thought she had chronic simple glaucoma. Nevertheless, mydriasis precipitated an acute attack of angle-closure glaucoma. I did not see the entire angle and I was misled into assuming that the remainder of the angle was merely hidden from view. The Gestalt phenomenon often plays tricks with our senses. To illustrate what is meant by gestalt: We may see only three legs of a table, but we assume that the fourth leg is there but hidden from view; yet, the fourth leg may actually be missing.

As Dr. Gorin pointed out, in an eye with a shortened angle the clinical picture often suggests chronic simple glaucoma; and so does the gonioscopic appearance, at least to an untrained eye. Yet, a careful history and appropriate provocative tests lead us to suspect angle-closure glaucoma. The presence of peripheral anterior synechias, on the other

hand, are adequate criteria for regarding the case as secondary glaucoma. The case thus has elements of all three types of glaucoma in varying mixtures. This explains why diagnosis is so difficult and often uncertain.

I want to say a word or two regarding the pathogenesis of shortening of the angle. It still remains a mystery why some eyes develop synechias in noncongestive angle-closure glaucoma, while most eyes do not. Possible factors favoring synechia formation are:

1. Presence of trabeculitis, or inflammation of the trabecular meshwork.

2. Abnormalities of endothelial cells of the trabeculae and of the iris opposite the trabeculae (dystrophy, desquamation).

3. Transudation of hyaluronic acid from the trabeculae into the anterior chamber, followed by fibroblastic proliferation.

4. Transudation of plasmoid fluid from Schlemm's canal through the trabeculae into the anterior chamber, followed by fibrin formation and eventually fibrosis.

This process of agglutination of the walls of the angle and subsequent fusion may be independent of the mechanism of angle closure. Of course, the proximity, and periodic contact of the walls of the angle favor this process. But it is by no means limited to eyes with narrow angles. An analogous process is observed more rarely but, nevertheless, in a sufficient number of cases to be worthy of note, in eyes with wide angles.

From my own experience I can divide these cases into three groups:

1. Aphakic glaucoma with deep anterior chamber, not caused by either delayed reformation of the anterior chamber or frank iridocyclitis. After uncomplicated intracapsular extractions, the angle may become filled by loose, pigmented tissue which resembles iris and bridges the angle. Glaucoma may or may not ensue, depending on how dense and how extensive is this tissue. My last two cases occurred in patients with chronic simple glaucoma whose tension had been well controlled for some time preoperatively.

2. Essential atrophy of the iris. In this condition I have observed the development of synechias from the formation of a few isolated fine threads bridging the angle to their coalescence and contraction, and finally a massive drawing of the iris toward the trabecular band.

3. Endothelial dystrophy which may be associated with mild uveitis, trabeculitis, or posterior embryotoxon. In endothelial dystrophy and posterior embryotoxon, synechias similarly bridge the angle and later contract, with the result that either Descemet's membrane becomes detached or holes form in the iris stroma, or both.

Finally a word regarding the treatment of eyes with shortened angles. Dr. Gorin has already emphasized the importance of using miotics even after iridectomy. It is not so much the contraction of the pupil as the stretching of the iris which helps prevent contact between it and the trabeculae, and thus counteracts the tendency to formation of synechiae. Early iridectomy is important, because after this operation the angle widens and the entire chamber deepens.

When performing the iridectomy, the incision should be made ab externo and should be placed at the limbus, not behind the limbus. The periphery of the anterior chamber does not extend two mm. behind the limbus as in the normal eye; in fact, it may not extend farther than Schwalbe's line in some sectors. If the incision is placed too far back, one is very apt to injure ciliary body, break the zonule and precipitate a malignant glaucoma. Within the past month I saw two cases of malignant glaucoma, both occurring after surgery for chronic noncongestive angle-closure glaucoma with shortened angles. Both cases I believe were attributable to placement of incisions two mm. behind the limbus. Both cases responded satisfactorily to lens extraction.

Skin grafting

Dr. Peter H. Ballen: Because of the reluctance of many ophthalmologists to enter upon substantial reconstructive work

around the eye, many of our patients will come under the care of those without training adequate to recognize eye pathology. This may lead to disastrous results. There should be no hesitation on the part of the eye surgeon in obtaining free skin, either split thickness or full thickness.

The best match for lid skin is skin from the fellow upper lid. Split-thickness grafts may be used where a larger area is needed than can be so supplied. The use of the electric dermatome is very helpful in taking thin split-skin grafts.

A motion picture showing the use of the Brown electric dermatome was shown. Lid adhesions were prepared and the scarred and distorted tissue of the lids (in the case of scarred lids following an infected stab wound) removed. The graft was then sutured into place.

A full-thickness graft was also pictured. It is important to dissect down to normal elastic tissue; finger exploration is better than visualization alone.

The procedures can and should be applied by ophthalmologists. Skill with the Brown dermatome is easily acquired.

Discussion. Dr. Sidney Fox reviewed the history of skin grafting. He agreed that ophthalmologists are the ones who should do this type of graft. He showed slides of cases where three and four lids were repaired by a single large split graft.

Dr. Byron Smith complimented Dr. Ballen on his presentation and on the absence of eponymic terms for full-thickness and split-thickness grafts. He prefers to use no lid adhesions; instead he puts the lid on a greater stretch by pulling on sutures placed along the lid margin. In this way a considerably larger graft may be used.

Mechanisms in convergence and divergence

Dr. Robert S. Jampel: It is generally believed that there is a "convergence center" in the third nerve nucleus in the midbrain, but there is little evidence for such a center and considerable against it.

Phylogenetically conjugate movements are a late development, occurring only in mammals.

Experimentally convergence can be produced by cortical stimulation but not unequivocally by midbrain stimulation.

Clinically convergence and divergence paralysis can occur in cortical disease.

Anatomically the evidence for the presence of and function of the "nucleus of Perlia" is very scant and mostly conjectural.

It is unlikely that a newly developed function would have a center in the "old" or midbrain. Complex functions like speech and chewing do not have a median midbrain-representation.

Dr. Jampel concludes, therefore, that convergence and divergence are integrated on a cortical level, there is no integrating or controlling center in the midbrain for them, and that the nucleus of Perlia is probably a myth.

Alan H. Barnert,
Recording Secretary.

OPHTHALMOLOGICAL SOCIETY OF MADRID

February 14, 1959

Dr. Marin Amat, *presiding*

Groenow type I nodular opacity of the cornea

Dr. Arjona: A woman, 64 years of age, complained of progressive loss of vision. Slitlamp examinations showed multiple centrally located small nodules of the corneal stroma in both eyes, separated from each other by completely transparent cornea. There was no ciliary or conjunctival hyperemia. The patient has a younger sister, aged 42 years, presenting a similar clinical picture but less advanced. Dr. Arjona Santos commented on the chemical composition of the nodules, the familial character and the relation to the type II or macular opacity of Groenow. He admitted the entity to be independent of lattice corneal dystrophy.

Discussion. Dr. Leoz de la Fuente said

he had a case of Groenow type II macular opacity on which he performed a corneal keratoplasty and will make a pathologic study of the cornea obtained.

Dr. Marin Amat reminded those present of the beautiful specimens of this entity shown by Prof. Fuchs in 1920 during his pathology course in Madrid and summarized the main differences of the nodular and macular type opacity—the nodular or Groenow type I is more circumscribed and hence impairs the vision less, the macular form is more diffuse. The first type is transmitted directly from father to child; the second in a recessive fashion from grandparents to grandchildren.

Both types are well differentiated from the lattice degeneration of the cornea.

March 11, 1959

Case reports

Dr. Leoz de la Fuente presented a case of diabetic retinopathy.

Numerous microphotographs were shown proving the similarity of the lesions of the retinal capillaries and those of the renal glomerulus. In both there was a hyaline degeneration of the internal layer of the capillaries, with deposits of fibrinoid degeneration. In a few of the slides sacular microaneurysms were seen communicating with the capillaries. Dr. Leoz reaffirmed that microaneurysms are not specific of diabetic retinopathy since they are seen in other diseases and even in a normal retina.

A photograph of a melanoma of the limbus was shown, which appeared to cover part of the cornea and seemed to penetrate the globe at the limbus. After enucleation it was demonstrated that the melanoma had not penetrated the eye.

Several microphotographs of leukemic retinitis were presented.

A photograph was shown of a case of dermatomyositis of the upper lid.

Another photograph demonstrated an erythematous lupus of the lower lid.

Several microphotographs presented a case of trico-epithelioma of the lid.

Rothmund syndrome

Dr. Soto spoke about two cases of Rothmund syndrome occurring in two brothers. The eldest, aged 22 years, presented café-au-lait spots spread over the body, diminution of vision, body underdeveloped, feminoid distributions of fat, testicular atrophy, and so forth.

There was bilateral aphakia (surgical) and osteoporosis.

The other brother, aged 19 years, presented a similar group of symptoms but less marked. Visual acuity was diminished, due to bilateral lens opacities.

Dr. Soto compared the syndromes of Rothmund and of Werner. Both syndromes presented visual and cutaneous lesions but in Rothmund's syndrome the cataract appears bilaterally in the first month of life and progresses rapidly, while in the Werner syndrome the cataract appears during the third decade of life.

Rothmund's syndrome follows a recessive type of inheritance while Werner's is of the dominant character. The cutaneous lesions of the latter syndrome closely resemble those of sclerodermia.

Discussion. Dr. Leoz commented that in the Werner syndrome the patient may present cataract and sclerodermia or the sclerodermia may be missing; that is, the inheritance refers not to the lesions themselves but to a predisposition to congenital anomalies. The difference between both syndromes is the chronologic order at which the disease manifests itself, showing endocrine, ocular, and cutaneous participation.

Dr. Bartolozzi inquired about the place of origin of the patients and the genealogy of the two brothers.

Dr. Soto replied that the patients are from Albacete and that he has no other family history.

Olga Ferrer,
Translator.

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DONDERS AND ASTIGMATISM

Donders was the first great ophthalmologist to investigate assiduously the problems of refraction and the first to impress upon the profession the prevalence and importance of astigmatism. His initial paper on this subject, which appeared just a century ago in Graefe's *Archiv,* introduced the term, "Astigmatismus" to the German language.

The primary discoveries relating to astigmatism were made by physicists and mathematicians. In 1670, Newton noted the astigmatism of oblique bundles of rays in spherical lenses in his lectures at Cambridge University. The celebrated blind mathematician, Leonard Euler, who flourished in the gen-

eration after Newton, worked out the currently used general formula of the power of cylinders at various angles from the axis and deduced from it that like cylinders at right angles are optically equivalent to a sphere of the same power. The first scientific use of a cylindrical lens was made by Fresnel in 1819 for the purpose of obtaining a luminous line.

In 1747, Porterfield invented an instrument which he named optometer for the measurement of simple myopia and hyperopia. The optometer, though now obsolete, is historically important. Young, while using his own optometer, was the first to reveal and measure the astigmatism of a human eye, in 1801. In 1827, the astronomer, George B. Airy, first utilized a cylinder for the correction of ocular astigmatism. However, another Englishman, John I. Hawkins, had the idea independently a year earlier. He wrote:

> Recently by the use of the optometer I ascertained that the indistinctness of my right eye is occasioned by the vertical focus of that eye being greater than the horizontal focus. I contemplate making a glass that shall show greater magnifying power vertically than horizontally, to accomplish which I shall avail myself of a plan patented by Chamblant of Paris, and make the surfaces of my glass segments of cylinders, one side vertical and the other horizontal.

In 1849, Airy reported a change in his eye; both the myopia and astigmatism had diminished. He referred to the latter as "a geometrical phenomenon to which the term astigmatism was very happily affixed by the present master of Trinity College, Rev. Dr. Whewell." Edward Jackson and Swan Burnett, however, preferred "astigmia," as this term is etymologically more correct and harmonizes with all other words relating to the optical condition of the eyes, such as myopia, asthenopia, esophoria, exotropia and so on.

The articles of Airy stimulated intellectuals in England and America to note their own astigmatism and to attempt correction. In 1828, John McAllister of Philadelphia ground a plano lens with a concave cylinder axis horizontal for Rev. Goodrich, which was the first ever made in this country.

J. C. F. Sturm, a Swiss mathematician, in 1845 published in French the first complete analysis of the refraction of light by an astigmatic system. In 1849, Stokes introduced a test based on two rotating cylinders of equal but opposite power. The idea survives now only as a malingering test in a simplified adaptation by Edward Jackson.

The ophthalmometer of Helmholtz, invented in 1854, permitted an accurate determination of the radii of the principal meridians of the cornea. Calculation showed that each millimeter of difference in these radii produced six diopters of astigmatism. An earlier device, the Placido disk of concentric rings, had proved useful in the detection of corneal asymmetries manifesting high astigmatism, irregular astigmatism or conical cornea. Extensive use of the Helmholtz ophthalmometer by Donders enabled him to demonstrate, in 1860, the hitherto unsuspected prevalence of significant corneal astigmatism. To learn the total astigmatism Donders used an optometer provided with a stellate figure borrowed from Helmholtz and measured the foci of the principal meridians. Astigmatism had been considered until then a rare anomaly and the remarks by Hays in 1854 concerning three patients of astigmatism fitted with lenses were considered noteworthy.

In 1862, Donders published in Dutch a 136-page monograph on "Astigmatism and Cylindrical Lenses" which was forthwith translated into German by Karl Schweigger and into French by Henri Dor. As a consequence of this work cylinders were henceforth added to the trial case.

Donders began by exploring the techniques then known for the clinical measurement of astigmatism—that of Young and Airy, respectively. As to the first, Donders concluded: "Determination of astigmatism by the optometer often produces variable results because of the difference of accommodative power of both meridians in two successive examinations." He then modified

Airy's procedure. With the patient viewing a remote point of light, spherical lenses were successively applied to bring out most definitely the stripe of light in each meridian. As the changes in the apparent form of the bright dot were often not readily recognized, Donders finally limited this test to the determination of the principal meridians, then placed a narrow slit at the axis of each principal meridian in turn. He wrote:

> In these two meridians, the strongest convex lens, or the weakest concave one by which the best distant visual acuity can be gotten, is to be employed. The degree of astigmatism is obtained by the difference of refraction in the two meridians. If emmetropia or hypermetropia be present in one of the meridians, it is well, so as to obtain a very exact result, to previously paralyze the accommodation by means of atropine.

Donders' book, *On the Anomalies of Accommodation and Refraction of the Eye*, published in English in 1864, is, in the words of Duke-Elder, "one of the few classics that have caused a revolution in ophthalmology." Donders emphasized that diminution of acuity was the most important symptom of astigmatism. Because of this, affected persons are obliged to read at a closer distance and hence suffer from accommodative asthenopia. In astigmatic patients, he wrote:

> There exists a certain indifference for (spherical) lenses. It is impossible to make a definite choice. This phenomenon led me long ago to suspect that the diminished acuteness of vision might be dependent on abnormal astigmatism.

A summarized revision of this book was published in Dutch in 1869 and translated into English in 1899.

Ophthalmologists flocked to Utrecht to study under Donders. Among these were Dyer of Philadelphia, Hasket Derby of Boston, and John Green of Saint Louis. After John Green arrived in 1865 he was inspired to devise a more reliable test for the detection and measurement of astigmatism. The astigmatic charts in optometers had been unsatisfactory because of the disturbing influence of accommodative efforts. To eliminate this factor he introduced large test-diagrams, hung on the wall at a distance of 20 feet. Among the variety of charts he devised are radiating lines, rotating dials, duplicated triplicated and dotted lines.

The Helmholtz ophthalmometer that led Donders to detect the prevalence of astigmatism was a laboratory contrivance that required numerous readings and tedious calculation. Javal and Schiøtz perfected an accurate but simplified instrument in 1884. As a consequence of this triumph of automation, the examination for astigmatism became widespread and the previous hesitancy in prescribing cylinders was vanquished. By 1894, cylinders were ground by machinery and the advent of the 20th century heralded the manufacture of toric lenses. Though flat lenses were cheaper, less conspicuous and caused less reflections, the superior performance of toric lenses gained such general acceptance that by 1920 the flat lens was almost obsolete.

Retinoscopy was discovered by Cuignet in 1873 but its principles were first elucidated by Landolt who, in 1886, christened it skiascopy or the shadow test. Shortly before this date, a paralysis of accommodation caused by diphtheria led Edward Jackson to read Donders. This masterwork so fascinated him that he gave up general practice for ophthalmology and soon became the Donders of America. His classic, "Skiascopy and its Practical Applications to the Study of Refraction," published in 1896, clarified the technique and emphasized its importance as the most accurate of all methods for the objective determination of the refraction, including the degree and axis of astigmatism. In 1893 Jackson announced his cross-cylinder test as a superior subjective method for determining the precise amount of astigmatic error and in 1907 he described the even more valuable cross-cylinder test for astigmatic axis. Familiarization with the shadow test and the cross cylinder caused the ophthalmometer and to a less extent astigmatic charts to follow into desuetude the op-

tometer, the cobalt-blue glass, and the stenopaic slit.

After 1900 the examination for astigmatism had become so commonplace that thousands of cases were analyzed by numerous authors. It was soon discovered that astigmatism was not a fixed quantity but varied with age; that a symmetry of astigmatism in both eyes was frequent, both in degree of error and in the direction of the axis; and the further the eyes veered from emmetropia, the more common was the occurrence of astigmatism. In 1899, Wurdeman proudly proclaimed: "We Americans certainly measure the refraction of the eye more closely, and have done more towards the study of it, than those abroad." Whatever the merits of the statement then, it is admittedly true today.

James E. Lebensohn.

Vth NATIONAL CONGRESS OF THE MEXICAN OPHTHALMOLOGICAL SOCIETY

The Vth National Congress of the Mexican Ophthalmological Society which was held from March 6 to March 10, 1960, in Mérida, Yucatan, has given renewed evidence that Mexican ophthalmology has come of age. The scientific program was excellent and consisted of six symposia and 37 individual papers, a rich harvest indeed.

Each of the symposia was organized by one of the great ophthalmologic departments of the capital. The first, on exophthalmos, presented by Dr. Enrique Graue and six members of his staff of the ophthalmic hospital, Nuestra Senora de la Luz, dealt mainly with the endocrine type of exophthalmos. Drs. Feliciano Palomino Dena and Renán Murillo Fajardo of the Ophthalmic Service of the Children's Hospital of Mexico spoke of "The present status of orthoptic treatment in strabismus." Dr. Luís Sánchez Bulnes and the staff members of the Hospital of the Association for the Prevention of Blindness in Mexico had chosen the rather unusual topic: "Ocular pigmentation in normal and pathologic conditions," giving an excellent survey of the problem, restricting themselves essentially to the melanotic pigment.

Unusual also was the topic of the third symposium: "Correlation between cerebral, ocular and manual dominance.'" This difficult subject was clearly and exhaustively discussed by Drs. Abelardo Zertuche, Francisco Arenas Bolaños and Guillermo Castro Riddle, all from the Ophthalmic Service of the Central Military Hospital in Mexico City.

A symposium on contact lenses in which the beneficial use of these devices in unilateral aphakia was particularly emphasized, was presented by Drs. Daniél Silva, Francisco Montellano, Mario Salcedo and Ignacio Rodríguez.

While all these symposia were more or less of the didactic type, familiar to us from our Academy meetings, the symposium presented by Drs. Magin Puig Solanes, Enriqueta Camacho and Juán Heatley, entitled "Gonioscopic and tonographic studies of the population of the Republic of Mexico: II. Study of Mestizos and Whites," discussed the results of an investigative study of unusual interest. These workers have followed up on the observation that glaucoma is unknown among the Indian population of Mexico and have made a careful study of the biomicroscopic and ophthalmoscopic appearance of the eyes and of their function in about 150 Indians of various groups and of 50 Mestizos. While their findings are still preliminary (they hope to collect data on 1,000 persons in each group), these findings nevertheless appear quite significant: the angle is extremely wide open and does not narrow noticeably with age; the average P_o is low (11.82 and 13.58 with the indentation tonometer, respectively, for Indians and Mestizos, and 13.73 and 13.99 with the applanation tonometer); the C values are normal (0.26 and 0.36, on the average, for Indians and Mestizos, respectively) as are the

values for scleral rigidity (on the average 0.0233 and 0.0206, respectively, for the two groups), but the values for F are quite low (1.04 and 1.34 $cm^3/mm.$ for the two groups). The authors of the report have not neglected the consideration of other factors, such as the great rarity of hypertensive cardiovascular disease among the Indians of Mexico, in the evaluation of their results. There can be no doubt that once their painstaking investigation is completed it will represent a truly monumental contribution to human comparative ophthalmology and to the glaucoma problem as a whole.

Among the contributed papers the large number (nine) relating to strabismus emphasized that the world-wide increase in interest in the neuromuscular anomalies of the eyes has also reached Mexico. Burian, as invited foreign guest, discussed recent developments in this field. Dr. Anselmo Fonte Bárcena spoke of diagnosis and treatment of strabismus and presented a paper on surgical results in 109 cases. Drs. Renán Murillo Fajardo and Graciella Novarro discussed the use of DFP in the treatment of comitant strabismus, while Dr. Bertha Riveroll Noble showed a film on the recession of the medial rectus muscle. Dr. Teódulo M. Agundis and his assistants, Dr. Francisco Montellano and Dr. Andrés Flores Hintz, gave three papers in which sensory adaptations, anomalous retinal correspondence, suppression and amblyopia were dealt with. An experimental paper by Dr. Jorge Sánchez Alonso, from the same group, was especially noteworthy. In it Dr. Sánchez reported on his studies of the central transmission time in amblyopia which he found to be 15 to 73 percent longer in the amblyopic eye than in the normal fellow eye.

But strabismus was only one of the many features that absorbed the attention of speakers and audience. Dr. Luis Sánchez Bulnes (with Dr. Flores) gave an up-to-date review of the present status of detachment surgery and this master of intraocular surgery also demonstrated a film in which the surgical removal of intravitreous cysticercus was shown, executed in virtuoso fashion. Dr. Torres Estrada delivered three papers dealing with glaucoma, the present status of our knowledge, the process leading to the formation of glaucomatous cupping and the aims and techniques of the surgical treatment.

A number of papers were concerned with other surgical aspects: the treatment of fistulas of the lacrimal pathways (Dr. Arcadio Chacón Mendoza), absent or delayed reformation of the anterior chamber (Dr. Raúl Franco Lara), akinesia of the extraocular muscles (Dr. A. Chacón Mendoza), instrumentation for cataract surgery and the supporting scleral ring of Flieringa (Dr. Juán R. MacGregor), care of surgical instruments (Dr. Leon Escobosa), sutures for hermetic closure of the incision in cataract surgery (Dr. A. Torres Estrada), an experimental study of enzymatic zonulolysis (Drs. Jesús M. Benavides and Ezequiel Cavazos), total corneal transplant in five cases (Dr. Diego Cuevas Cancino).

Among the other papers two by Dr. Juán Heatley were of special interest. One dealt with gonioscopy in processes other than glaucoma. The essayist emphasized the inestimable value of the slitlamp in gonioscopy and made a plea for the routine use of gonioscopy. The second paper, with Dr. Sadí de Buen, recorded a family with congenital miosis, an extremely rare occurrence. It was demonstrated in an excised piece of iris from one of the members of the family that there was a complete absence of the dilator muscle. Dr. Sadí de Buen, who is a general pathologist specializing in ophthalmic pathology (he has spent three and one-half years at the Armed Forces Institute of Pathology, Washington, D.C., for this purpose) but who is also professor of histology at the Medical School of the National University in Mexico City, spoke of the ocular histopathology in malignant arterial hypertension. His material came from a large

number of autopsy cases. He is continuing to collect autopsy material from all types of patients and this collection should become, for many reasons, of outstanding value to the study of the normal and pathologic anatomy of the eye.

The use of vitreous injections was discussed by Dr. E. Graue (he prefers this designation to the more common term "vitreous implant") and a technique for the production of better prostheses was described, and illustrated by a film, by Drs. Carlos Zaldívar and Enrique Graue. Dr. Manuel de Rivas Cherif spoke of the retinal vascular index of Onfray, Dr. Fernando E. Rosas Marín of retinal dysplasia, Dr. Pablo Zaldívar of lid tumors, Dr. Alfredo Gomez Leál of the histopathology of conjunctival tumors and Dr. Aurora Miranda of their surgical and radiation treatment. Dr. Juán Salazar Salazar gave a paper on the treatment of the pterygium with beta rays and Dr. Enrique B. López Quiñones one on the present-day treatment of blepharitis. The same essayist, together with Dr. Ricardo Fernández, considered the tubercular ocular manifestations in the State of Sonora; the chemical investigation of new steroids used in ophthalmology was presented by Dr. Octavio Mancera; and the prevention of eye accidents to workers by Drs. Renán Murillo Fajardo and Eduardo Mendoza Tapia.

In spite of this strenuous schedule of scientific presentations which was carried out with remarkable efficiency, the social aspects were not neglected. Various meals in most pleasurable surroundings and more particularly excursions to the famed ruins of Mayan cities, unique in their grandeur, gave the opportunity for close personal contact among the members of the congress and contributed greatly to making this event an unforgettable experience.

The social affairs were no less well organized than the scientific sessions for which much credit is due to the members of the Local Committee, to its presidents, Drs. Fernando López Rodriquez and Carlos López Alonzo, and especially to its indefatigable secretary, Dr. Efraím Acosta Acosta. It is because of this smoothness of organization that the whole congress evolved in an atmosphere of perfect relaxation, though we were kept busy every waking minute, and that it was an unqualified success.

Hermann M. Burian.

OBITUARY

JOSÉ MANUEL ESPINO
1885-1960

On the evening of February 5, 1960, at the end of the VI Pan-American Congress of Ophthalmology, the last activity in his long ophthalmologic career, Dr. José Manuel Espino died.

At the same grounds where the Congress was held, surrounded by the love of his devoted wife, by the sorrow of his Venezuelan disciples and by the surprise, from his sudden departure, of all his Pan-American confreres he passed away when getting ready

José Manuel Espino

for the closing banquet of the VI Pan-American Congress of Ophthalmology.

Dr. Espino was born in Guasipati, Bolivar State, Venezuela, November 23, 1885. After his primary school in Zaraza, Guárico State, he came to Caracas and received the degree of Bachelor in Philosophy and Sciences at the Central University of Venezuela, Caracas, in 1902, and the degree of Doctor in Medical Sciences from the same Institution December 5, 1908.

After several years of general practice Dr. Espino decided to specialize in ophthalmology. He received his training at the College of Physicians and Surgeons, University of California in 1915, and at Philadelphia Polyclinic, Wills Eye Hospital, Philadelphia General Hospital in 1916. Later he took courses in eye surgery at the University of Paris, Faculty of Medicine.

Dr. Espino was an indefatigable student and through his frequent traveling, systematic reading, and organized correspondence kept himself informed of the advances in his speciality.

Returning to his own country after training, he started his practice of ophthalmology and became interested in teaching. In 1918, he initiated the Catedra Libre of Ophthalmology and in 1931 was appointed professor of ophthalmology at the Central University, Caracas, a position he held until his retirement in September, 1948. From that date until his death he was honorary professor of ophthalmology of the Central University of Venezuela, Caracas.

More than 70 papers on different facets of ophthalmology are his contribution to our specialty and his *History of Ophthalmology in Venezuela* is unique in his country. He was a member of 21 medical and ophthalmological societies. He was president of the Venezuelan Academy of Medicine and one of its most active members. For his merits as a teacher he received several medals, the most recent, The Andres Bello Medal, on the 50th anniversary of his medical graduation.

If his teaching and writing were fruitful, if his knowledge was great, so the influence of Dr. José Manuel Espino on Venezuelan ophthalmology and on Venezuelan medicine was felt through his personality as well. His upright conduct in all the acts of his life, his gentle manner of handling even the most difficult task, and his personal knowledge of man's nature were the tools in his hands, that molded (by himself, without knowing it) the most beautiful monument to his memory—the admiration, recognition and appreciation of his many pupils and friends.

The passing of Dr. José Manuel Espino leaves in the ophthalmology of the Americas and in Venezuelan ophthalmology, particularly, a collection of memories that permit us to say: he was a great man!

Dr. Espino is survived by his beloved wife, Mrs. Delia de Espino, and by his son José Manuel.

R. Cordero Moreno.

CORRESPONDENCE

Cause and cure of entropion

Editor,
American Journal of Ophthalmology:

The January, 1960, issue of THE JOURNAL contains an article by Dr. Lester T. Jones entitled "The anatomy of the lower eyelid and its relation to the cause and cure of entropion." This is a carefully planned piece of work, such as we have learned to expect from the author's previous contributions.

I shall not comment on Dr. Jones' exposition of the subject, nor shall I presume to express an opinion as to the surgical procedure which he espouses, much as I would like to do so. After all, he has charitably managed not to comment on my few contributions to the subject of senile entropion. Can I be less generous?

But I do wish that he had been just a bit more assiduous in the perusal of his ref-

erences. Knowing how meticulous he is in his anatomic dissections, I am sure that he must have allowed some one else to do his bibliographic research. Nothing else can account for some of the errors of fact that have crept into his work. For instance, I am sure that Dr. Jones would never have failed to notice that:

1. In his orbicularis transplantation operation, Wheeler resected preseptal muscle and not pretarsal muscle as Dr. Jones states in his article. In the description of his first procedure Wheeler says, "A strip of orbicularis muscle 4 mm. wide is dissected free just *below the lower border of the tarsus.*" Then in the modification of his original procedure Wheeler states, "This strip is taken just *below the lower border of the tarsus.*" (italics mine). He then directed that the muscle be sutured to the tarso-orbital fascia. This is what Dr. Jones advises now be done all over again.

2. Butler's procedure had a long-forgotten progenitor by the name of von Graefe who reported resection of an apex-up triangle for "entropion spaticum" back in 1864.

3. Reeh's modification (of Butler's operation) also removing a triangle of skin below the outer canthus is also of ancient lineage. Skin resection below the external canthus was suggested by a fellow named Fox in 1951. But let it not be said that a Fox ever got unmerited credit; for this (alas!) is not original with him either. Busch (1858), Goldzieher (1908), Blaskovics (1923) and others all rediscovered the same type of operation.

However, in that same 1951 article Fox, more importantly, included preseptal muscle with his skin resection. This was modified in 1952 so that even more preseptal muscle is now resected. It is this which Dr. Jones now advises be done as if it were something new.

4. In discussing the Gaillard and Snellen sutures Dr. Jones has them "emerge in the infraorbital region as described by the authors." For almost one hundred years Snellen's suture for entropion has been emerging just below the lash line of the lower lid. However, this is a niggling error, of small consequence. For, no matter how you place them, sutures (like ignipuncture and some of the other procedures Dr. Jones mentions) are as a broken reed in the repair of senile entropion.

It might be said—and with truth—that these are minor flaws in a work of this sort. But to paraphrase Mr. Dooley, "facts is facts." They are stubborn things. You may brush them aside, forget them, ignore them, or twist them but the pesky things will not stay buried and will out. I can speak feelingly and with authority on this subject because of my own sad personal experiences in the past.

I am sure that the last word on senile entropion has not been said. And it is good to see Dr. Jones take an interest in the subject. Who knows? Some day we may yet find the perfect solution to this vexing problem.

(Signed) Sidney A. Fox, M.D.
New York.

* * *

DR. JONES' REPLY

Editor,
American Journal of Ophthalmology:

I have read with interest the letter from Dr. Sidney A. Fox, written to you regarding my article, "The anatomy of the lower eyelid and its relation to the cause and cure of entropion," in the January, 1960, issue. A critic is really your best friend for he not only detects your weaknesses but tells you about them. He has pointed out some errors which I will comment upon.

Dr. Wheeler makes the exact statements reported by Dr. Fox, as I well know. But if Dr. Fox had read the full text he would have found that Dr. Wheeler, in the discussion, was asked how he isolated the muscle strip which he shortened in the simplified method. He stated, "I prefer to . . . with the scissors, cut down against the tarsus against

which the strips are outlined, etc." This, of course would *have* to be pretarsal muscle. This was the way I was taught to do the operation and the way I have observed others do it. Now why do you suppose Dr. Fox's researchers left this out?

The remaining three points largely deal with precedence, etc., which often cause considerable argument and injustice to the original author. I agree with Dr. Fox. But such things seem inevitable, for Dr. Fox himself has committed this offence in his article on entropion. For instance he mentions "Horner's" muscle. This is grossly unjust to Duverney who described it years before Horner did. Besides, a more correct name for it is the "deep head of the pretarsal muscle." Dr. Fox refers to the "tarso-ligamentous sling." This is a major anatomic blunder. Neither tarsus has a ligamentous attachment. The pretarsal *tendon* holds each tarsus firmly at its lateral end and the superficial head of the pretarsal muscle spans the gap between tarsus and medial palpebral ligament medially. This latter point was well worked out by Gerlach, Henke and others nearly 90 years ago. I also reviewed it over three years ago.

The purpose in reviewing older procedures in my entropion article was not to offer anything original but to try to apply valid anatomic reasoning to what was done. On this basis I would humbly hazard a guess that Dr. Fox would have just as good results in his operation if he forgot to resect the triangle from the tarsal plate and instead, concentrated on his resection of skin and muscle at the lateral canthus. If he shortens the preseptal muscle so it will be tight against the septum orbitale and transplants it downward far enough so it cannot override the pretarsal muscle above (as I'm sure he does) he should have as good results.

I shall deeply regret it if I have added to the "sadness in his personal experiences," and I would like to offer this bit of philosophy from Shakespeare to sooth his feelings:

Time hath, my lord, a wallet at his back
Wherein he puts alms for oblivion,
A great sized monster of ingratitudes:
Those scraps are good deeds past; which are devoured
As fast as they are made, forgot as soon
As done . . . Oh! Let not virtue seek
Remuneration for the thing it was, for beauty, wit,
High birth . . . desert in service . . . are subjects all
To envious and calumniating time.

(Signed) Lester T. Jones, M.D.,
Portland, Oregon.

Bayadi's convex glass

Editor,
American Journal of Ophthalmology:

In The American Journal of Ophthalmology (**48**:783 [Dec.] 1959), Dr. Rosen recommends Bayadi's convex glass for biomicroscopy of the fundus. He writes in his article:

"It should be pointed out that in the recent treaties by Busacca, Goldmann and Schiff-Wertheimer upon the biomicroscopic examination of the vitreous and the fundus, very little space is devoted to this lens in the 373 pages of the monograph. Goldmann raises the objection that this plus lens requires a greater space between the examined eye and the microscope than does the Hruby lens and that the present biomicroscopes do not allow for this increased spatial difference."

That is correct—if one stops reading the book at page 24. Pages 29 to 72 contain the chapter on geometric optics of the devices used for biomicroscopy of the vitreous and the fundus; pages 65 to 71 are concerned with the Bayadi glass (to the three-mirror contact lens only three pages are dedicated). There Dr. Rosen will find a discussion of the advantages and disadvantages of Bayadi's glass and also the reasons why we generally do not use it, though the new slitlamp of the firm Haag-Streit allows very easily its application: (1) vitreous structures can not be seen well with this device, (2) the surface of the normal central fundus is seen

convex, protuberant against the observer with Bayadi's glass while in reality it is concave. Flattening or change from concavity to convexity of the surface of the choroid can very easily be seen with an appropriate contact lens. With Bayadi's glass all these differences in surface form mean only small changes in convexity. Therefore slight diffuse prominences of the choroid cannot be detected with Bayadi's convex glass.

(Signed) H. Goldmann,
University Eye-Clinic, Berne.

* * *

DR. ROSEN'S REPLY

Editor,
American Journal of Ophthalmology:

Professor Goldmann has bestowed a signal honor in taking time to comment upon this article. It is with sincere humility and undisguised trepidation that I undertake to answer his comments. Since receiving his monograph, about two years ago, I have kept this wonderful book constantly before me, and while I cannot follow the physiologic optics, even were it not written in French, one may be assured that I am readily familiar with the beautiful pictures which appear in this manual, and with some of the more easily translatable paragraphs.

My purpose in writing the paper was primarily to call this method to the attention of those who are clinically interested and who are willing to try. If the method has any clinical value it will soon demonstrate itself, for there are many conditions where a contact lens cannot be used, and where the Hruby lens is inadequate. Certainly, in these cases, there is an indication for the convex preset lens and, as this is employed, its value and facility will become apparent. To avoid an error primarily of communication, I would like in self reproach, to restate the sentence which probably provoked Professor Goldmann's comments, and say "very little space is devoted to the *clinical use* of this lens." I have attempted clinically to utilize what researchers have offered theoretically, but I must allow the solution of the optics to Drs. Rotter and El Bayadi, who deserve the credit for pointing out the value of the lens. There is little doubt that what Professor Goldmann states theoretically is completely accurate; however, from a practical point of view, I have not found the distortions or the difficulties mentioned with the technique I am using.

There have been four new developments in this technique, each of which adds further to the utility of the method. These are:

a. The aspheric lens (Volk "conoid" or Keeler type—also recommended for indirect ophthalmoscopy).

b. A lens with scleral depressor such as is used in indirect ophthalmoscopy upon a thimble.

c. A special mobile chinrest so that the head may be moved farther from the microscope.

d. Compensatory prisms upon the oculars to keep the images together.

I can definitely state that when one uses this aspheric lens (in an average case) and focuses carefully and sharply upon the fundus, a very clearcut linear nonbulging beam can be made to run right through the disc, of hairline thinness (about two and one-half times the length of the disc). Going through the disc, this line dips down nicely into the physiologic cup. Since it is only two and one-half times the size of the disc, it could not cause very much distortion in such a small sector of the overall orbital arc, and one should not miss an area of edema or protrusion if he is able to follow a small pit in a disc. (It is quite evident that scleral pressure will cause a much greater bulge.)

While the original article endeavored not to emphasize the value of the lens in examination of the vitreous, it may be of interest to note that the very deep vitreous is accessible to this method and is very well seen, but again, the distance from eye to microscope must be increased.

I had been using the convex preset lens for several years before the publication of Professor Goldmann's monograph and was aware of the greater difficulty in examining "hyperopes" as mentioned by Dr. H. Rotter, but not nearly to the degree emphasized by Goldmann.

On occasion I have communicated with Hans Rotter upon problems of the "preset convex lens." He was much in favor of it, especially in "myopes." However, early in 1958, he informed me that the new "Haag-Streit 900" slitlamp would soon be available and would solve most of these problems. Nevertheless, it occurs to me that there still exist two unsolved problems: (1) the ability to move the chinrest away sufficiently from the microscope, (2) the preset convex lens should not be fixed, it must be angulated, tilted, moved in and out, just as is done in indirect ophthalmoscopy.

One of the difficulties with the Haag-Streit instrument is the inability to move the chinrest far enough away from the microscope. The further the chinrest is moved, the weaker the auxiliary plus lens necessary. A plus-32 aspheric lens supplied by Keeler gives a most beautiful picture and is completely free of distortion.

I am exceedingly grateful to Professor Goldmann for calling these matters to task, for I have always held every statement which he renders with filial reverence.

It is hoped that this extricated Egyptian lens may survive preliminary testing.

(Signed) Emanuel Rosen,
Newark, New Jersey.

Red glass and green light for cover tests

Editor,
American Journal of Ophthalmology:

It is often of great help in both diagnosis and treatment to observe the movement of an eye under cover while fixation is accomplished with the other eye. In my experience, I have found that the use of a white light and an opaque cover requires the examiner to take a somewhat awkward position to observe the covered eye. Because of the difficulty in looking behind an opaque cover, I have found that a green-colored flashlight and a red glass cover allow the examiner to look directly at the covered eye since the green light is opaque when viewed behind the red glass but the covered eye is easily seen by the examiner through the red glass. I have found a convenient source of these colored filters are the spectacles from the Worth-dot fusion test.

(Signed) Robert A. Sills,
Los Angeles, California.

Recording for the Blind, Inc.

Editor,
American Journal of Ophthalmology:

Recording for the Blind, Inc., 121 East 58th Street, New York 22, records each week the two-page section "The News of the Week in Review" from the Sunday edition of the *New York Times*. The entire news summary is contained on one seven-inch pressed disc recorded at 16⅔ rpm, playable on the Talking Book machines loaned free to the blind by the Library of Congress, or on any commercial record player using this speed.

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(Signed) Recording for the Blind, Inc.,
121 East 58th Street,
New York 22, New York.

BOOK REVIEWS

OCULAR VERTICAL DEVIATIONS AND THE TREATMENT OF NYSTAGMUS. By J. Ringland Anderson. With a Foreword by Sir Stewart Duke-Elder. London, British Medical Association, 1959, edition 2. Price: 42 shillings.

Anderson's well-known monograph entitled "Ocular Vertical Deviations" which appeared in 1947 as Monograph Supplement XII to the *British Journal of Ophthalmology* has now been republished in a second edition.

The designation "second edition" should be taken with a grain of salt. While the basic arrangement has remained unchanged, this is really a new book. The size has been expanded from 107 to 189 pages but, since the typeface has been altered, the actual increase in the volume of the text is greater than these figures would indicate. The number of illustrations has grown from 37 to 60.

The interpretation of the vertical deviations of the eyes offers many complex and puzzling problems. Their diagnosis and treatment is often difficult even for the seasoned ophthalmologist. The author does not skirt or minimize these problems and difficulties. In his monograph all phases of the subject are carefully considered. The types and causes of the vertical deviations, the disturbances of the vertical movements of the eyes and the anatomy and actions of the ocular muscles are discussed. As is natural, the sections on the palsies of the vertical muscles constitute the bulk of the volume (pp. 56-125). The chapters on the investigation, prognosis, and treatment of vertical disorders will be particularly welcome to the readers looking for information about these complex topics.

Anderson gives us a very complete, meticulous analysis of the pertinent literature, juxtaposing and weighing with great fairness the differences of opinion which are so prevalent in this field. The comprehensive view which the reader gains from this survey in itself makes the reading of the book a most worthwhile experience.

This is the more true since there have been some rather interesting developments in the field of the vertical deviations during the past 15 years, all of which are scrutinized. The new findings with regard to proprioceptive elements in the ocular muscles, the "eye centering system" of Bender, the work of Zeeman, Roelofs and Keiner on the optomotor reflexes, the new attempts at explanation of the dissociated vertical deviations, all are given due consideration. The findings of electromyography are used wherever they are pertinent to the argument and the so-called A- and V-syndromes are extensively treated. With regard to the latter, Anderson inclines to the view that they may change with age, that they may be satisfactorily treated with operations on the horizontal muscles and that a new deviation may be produced if the inferior oblique muscles are unnecessarily weakened. The final chapter deals with the surgical treatment of congenital nystagmus which is also an acquisition of recent years

to which Anderson himself has made original contributions.

The book is compactly written. Each sentence counts. It must be read with attention and concentration. Yet it is never dull and reads easily. Anderson has succeeded in infusing it with charm and wisdom. If one were to find fault with it, it would be that the author is far too modest in presenting and emphasizing his own views. Whenever they are expressed it is obvious that they are based on much thought and a wide clinical experience.

The volume is excellently bound, the illustrations are clear and well reproduced and the typeface very pleasing. No ophthalmologist who is looking for guidance in the field of vertical deviations of the eyes, and through the maze of the literature about this subject, should overlook Anderson's new monograph.

Hermann M. Burian.

DOCUMENTA OPHTHALMOLOGICA. Advances in Ophthalmology. Edited by von Bahr, Bietti, Ten Doesschate, Fischer-von Bünau, François, Goldmann, Müller, Nordmann (secretary) Schaeffer, and Sorsby. The Hague, Netherlands, Dr. W. Junk, Volume XIII, 1959. 516 pages, numerous tables. Price: Guilders 75.

After obituaries on Girolamo lo Cascio, ocular physiologist of the Faculty of Naples, by Bietti, and André Magitot of Paris, by Nordmann, the rest of the volume consists essentially of reports and papers presented before a Symposium on Glaucoma, organized by Prof. R. Weekers under the aegis of the University of Liege, September 2-6, 1958, just prior to the meeting of the XVIII International Congress of Ophthalmology in Brussels. Twenty-six scientists, internationally known for their work on glaucoma, took part in this significant meeting. The papers are published in English, French, and German, according to the author's choice (with summaries in these languages).

The symposium is divided roughly into four parts: (1) the formation and elimination of the aqueous humor; (2) the neuromechanism of control of intraocular pressure; (3) tonometry and tonography; (4) perimetry and the early diagnosis of primary glaucoma. The conclusions are masterly, set forth by Goldmann (in German). It can be said with confidence that the papers exhibited in this symposium are of great scientific value and express in all detail the thoughts and work of these outstanding scientists who are combining their modern clinical and laboratory studies of this complex subject for our benefit. The papers are not simple or easy to read but the discussions that subsequently ensue help very much to clarify the topics.

The volume ends with:

1. A discussion of modern ophthalmodynamometry by A. Lobstein and J. Nordmann (in English). It is an excellent discourse of the subject which has created world-wide interest and enthusiasm recently. The authors' summary includes the following statement: "Dynamometry provides exact information in the diagnosis of occlusions and stenoses of the carotid system. It affords a means of increasing the security and efficacy of carotid ligation in the treatment of intracranial aneurysms. In the case of arterial hypertension, the cerebrovascular resistance may be estimated in some measure."

2. Investigations on the coefficient of (ocular) rigidity by J. Draeger of Hamburg (in German). This author found a typical decrease of the coefficient of rigidity with increasing age, as well as a significant increase of intraocular pressure with age.

3. The frontal reference surfaces of visual space by Thorne Shipley, Miami, Florida (in English). This is essentially a critical review of the experimental literature on the frontal reference surfaces of binocular visual space, with "particular concern for their change of shape as a function of the observation distance." The term "horopter"

is shown to cover several fundamentally different reference surfaces. Further experimental work is needed.

Most ophthalmologists are by this time familiar with *Documenta Ophthalmologica* of which this is the 13th volume. The present work continues to display the high scientific value of its predecessors, emphasizing, as they do, the basic scientific studies currently going on in ophthalmology, and is essential for the understanding of our science.

Derrick Vail.

DER AUGENARZT: VOLUME II. By Karl Velhagen (with the collaboration of the late W. Comberg, G. Günther, A. Heydenreich, W. Kyrieleis, F. Müller, F. Peiker, R. Sachsenweger, E. Schmöger, and H. Schober). Leipzig, Georg Thieme, 1959. 901 pages, 435 illustrations, some in color. Price: DM 122.30.

The second volume of this monumental project follows the pace set in the first volume which was reviewed in THE JOURNAL last year (47:257 [Feb.] 1959). Karl Velhagen outlines the procedures to be followed in taking the history. The significance of the symptoms mentioned by the patient is explained briefly. A general synopsis of the methods of examination and the principles of therapy which are of interest to the ophthalmologist merely serve as introduction to the chapters which follow. American ophthalmologists unfamiliar with the practice of their European colleagues will be surprised to learn the reason for the omission of a detailed discussion of the surgical procedures: the majority of European ophthalmologists do not perform major surgery!

Andreas Heydenreich discusses the methods of examination of the anterior segment of the globe; the position of the eye in relation to the orbit; ophthalmoscopy; diaphanoscopy; and ophthalmodynamometry. There is a brief concluding section on anterior segment and fundus photography. One can but marvel at the ingenuity of some of the newer methods, most of them presented in great detail. The majority of these procedures are perhaps only tools of research today, but one wonders if some of them might not be destined to become a matter of routine in the clinic or office of tomorrow. Only a few random examples can be selected. Kornerup developed a method for the objective evaluation of the inflammatory changes of the eye by determining the oxygen concentration in the pericorneal vessels under monochromatic light. The quantitative examination of the corneal sensitivity has been elaborated by a number of authors in the form of various modifications of Frey's hairs. Most widely used seems to be the instrument described by Boberg-Ans.

The various types of currently available European slitlamps, including the 900 model of the Haag-Streit slitlamp, are discussed. There is a more than adequate presentation of the technical principles of the use of the slitlamp, including colloidometry, the various means of determining the depth of the anterior chamber, and the technique of posterior slitlamp microscopy.

Schenk has developed a unique method for the localization of inaccessible retinal tears. He uses a high frequency electrode and a photoelectric cell. After the ophthalmoscope has been focussed on the tear, the photoelectric cell is brought to a corresponding area on the outside of the sclera. The photoelectric effect is changed to an acoustic signal which becomes the louder the more accurately the cell is placed. Once the optimum position is reached, it is marked with the electrode.

There is an extensive discussion on ophthalmodynamometry. Of special interest is the angiotonometer, an instrument constructed by Baurmann; it allows the direct reading of pressure in mm. Hg.

The late Wilhelm Comberg contributed a masterly introduction to the testing of the light sense. Not only older methods—some of them mostly of historical interest—but

most of the currently used instruments are discussed. The universal adaptometer of Goldmann-Weekers receives a well-deserved special consideration.

The methods and instruments for the examination of the visual field are discussed by Herbert Schober. Although the significance of the size and brightness of the test objects is stated, a more adequate explanation of the importance of determining a number of isopters with different variables would have been highly desirable in a text of this sort.

The chapter on the pathology and clinic of the anomalies of refraction by Rudolf Sachsenberger is a delight. Although his extensive statistical data may not add anything new, they are presented in a most stimulating fashion. Rushton's method of determining the axial length of the globe—especially the data collected by Stentström—is highly illuminating. There are beautiful illustrations of the myopic fundus, as well as an excellent description of the anatomic changes. The surgical treatment for myopia—shortening of the globe, Fukala's operation, anterior chamber lenses, and Sato's procedure of scarring the posterior surface of the cornea—is outlined in an objective manner, pointing out the questionable advantage and the enormous danger inherent in all of these techniques.

The chapter on aniseikonia is adequate and without too many details. Since the basic work was done in this country and since there does not seem too much enthusiasm for this subject in Germany, these pages offer nothing worthwhile not available in the American literature.

Werner Kyrieleis contributes a chapter on the pupil. His is a rather complete treatise. Thus it is surprising that he does not mention the pharmacodynamic method of Foerster and Gagel for the localization of the lesion in Horner's syndrome or the use of Mecholyl® for the diagnosis of the Adie pupil, as suggested by Scheie.

Elisabeth Schmöger actually presents a monograph on roentgen diagnostics for the ophthalmologist—in the opinion of this reviewer the highlight of the entire volume. This chapter deserves to be published as a separate edition, a distinction which has been awarded to two chapters of the first volume. An English translation would be a real boon to our literature, and of equal benefit to the ophthalmologist and radiologist.

Schmöger's suggestion that the optic canal can be demonstrated best in a stereoscopic view cannot be too strongly endorsed. She stresses that the optic canals of the tower skull are tilted, not narrowed—a frequently forgotten fact. For the visualization of the tear passages, as well as for orbitography, she recommends aqueous rather than oily iodine solutions, although she cautions to use orbitography only as a last resort because of the dangers inherent in the procedure.

The following chapter by Franz Peiker is on physical therapy related to ophthalmology. Since hydrotherapy, balneotherapy, and climatic therapy rightly belong in the domain of certain cultists it is hard to understand why this chapter was included. It certainly seems an anachronism to discuss seriously the so-called "Eichotherm" and its use in chromotherapy: light-orange light is recommended for blepharitis and chemical injuries to the cornea and sclera; red light for dacryoadenitis; and blue light for painful burns and neuralgias! Even iontophoresis, which receives a very excellent presentation, has lost the certain popularity it enjoyed a decade or so ago.

Fritz Müller treats the diseases of the lacrimal apparatus in a suitable manner.

Schmöger's discussion of clinical electroretinography maintains the high level set in her chapter on roentgenology. She urges to include in all publications data on the type of stimuli and leads, as well as on the amplification and registration. A number of authors, among them Karpe and Straub, publish findings with acceptable standards.

In her opinion the instruments in common use are not well enough standardized, with the exception of Karpe's electroretinograph. She gives a very detailed description of her own equipment which certainly leaves nothing to chance. Part of it is an EEG machine which permits the simultaneous recording of both eyes or of each individual eye.

An interesting observation is mentioned in the discussion of the pathologic ERG: a negative ERG is a rare finding in branch thromboses of the retinal vein. If present, the prognosis is poor—even if the vision is satisfactory. If, however, the ERG does improve and approximate the normal tracing during the course of the disease, the blood supply of the retina is satisfactory, and the outlook favorable.

Georg Günther writes the concluding chapter dealing with diseases of the sclera. It is quite brief. In particular, one misses a more detailed description of some of the histologic findings.

In summary, it can be stated that the high level established in the first volume is maintained here, almost throughout. It seems to be evident that the purpose of this undertaking is not so much a complete coverage of the entire field of ophthalmology as a detailed presentation of selected subjects in essay form. Nevertheless, the two concluding volumes may supplement some of those topics which so far seem to be somewhat incomplete, thus giving a more comprehensive coverage of the entire field of ophthalmology.

Stefan Van Wien.

ATOPIC CATARACT. By Emanuel Rosen, M.D. Springfield, Illinois, Charles C Thomas, 1959. 100 pages, 17 illustrations, bibliography, index. Price: Not listed.

This is one of the American Lecture Series, published by Thomas, and one of the American Lectures in Ophthalmology, edited by Donald J. Lyle, M.D., of Cincinnati, Ohio. The author is lecturer in biomicroscopy at the Newark Eye and Ear Infirmary. In this well-written and printed monograph he has attempted to clarify the confusing and complex subject of the relationship of a more or less characteristic type of cataract in some patients suffering from atopic dermatitis. He is, I think, successful in this attempt, although much more knowledge is required before we can close the book, ring the bell, and blow out the candle.

The author outlines the history, the "cutaneous story," the early and biomicroscopic findings, rate of development of the cataract, incidence, bilaterality, types (43 percent are "shield" shaped), and surgical complications (high incidence) in a review of 244 cases found in the literature. Chapter 6 concerns four theories relating to the pathogenesis. Then follows an important chapter on differential diagnosis; next a good discussion of surgical prognosis. Chapter 9 is a general and thoughtful discussion of the whole study. The final chapter consists of detailed reports of 10 cases studied by the author.

Atopic cataracts are probably more common than is realized and the surgery of the affected lens is fraught with dangers and difficulties. This monograph, although it could have appeared as a paper in one of the scientific journals, deserves praise for spotlighting the problem not only for ophthalmologists but also for our colleagues in general practice, dermatology, allergy, psychiatry, and immunology. It is a useful little book for study and reference.

Derrick Vail.

TREATMENT OF CANCER IN CLINICAL PRACTICE. Edited by Peter B. Kunkler and Anthony J. H. Raines. Edinborough and London, E. and S. Livingstone, Ltd., 1959. The Williams and Wilkins Company, Baltimore, exclusive U. S. agents. Price: $19.00.

It is evident that the treatment of cancer cannot be fully discussed in a single volume and that there are few practitioners likely

to be either in the position to treat or to have the spirit to manage all the malignancies which may occur in the various body organs and anatomic areas. However, because of the specialization required to treat cancer, physicians may not be aware of the advances taking place in fields other than their own. Thus, in this new text, edited by a radiotherapist and surgeon, a large number of contributors collaborate to present their views concerning the treatment of cancer. A surprising variety of material is presented, varying from the physics of radiotherapy to general surgical methods, to chemotherapy and hormonal control. Generally the most recent advances up to 1957 are presented.

The section on the eye and orbit is most competently presented by Dr. Arthur B. Jones, the deputy-director of the Radiotherapeutic Department of St. Bartholomew's Hospital in London, and ophthalmologist H. B. Stallard. The discussion, as might be expected from these authorities, is unusually well presented, and much information which is scattered through the literature concerning the technique of radiotherapy and the surgery of malignancy of the eye and orbit is included. If the remainder of the book presents the principles of therapy as concisely, authoritatively, and scholarly as the section on the eye and orbit, it may be considered a well-nigh flawless text. It seems likely that this book will become a standard reference for the therapy indicated for cancer by those seeking a survey of fields other than their own.

Frank W. Newell.

TRANSACTIONS OF THE AMERICAN OPHTHALMOLOGICAL SOCIETY, 1959: Volume 57. Toronto, University of Toronto Press, 1960. 737 pages, index. Price: Not listed.

Dr. Verhoeff's lead article in this volume again points out that the "Young Turk" spirit is completely unrelated to chronologic age. "Panum's area and some other prevailing misconceptions concerning binocular vision" bristles with indignation at the acceptance of historical authority (other than Dr. Verhoeff). His essential thesis is that binocular vision is primarily a subconscious function elaborated in the cerebral cortex and not in the eyes. Only Dr. Derrick Vail had the courage to discuss this paper and he studiously avoided any controversial comment. *Un homme de discrétion.*

Dr. Bedell discussed "Ophthalmoscopically visible small spots in the ocular fundus." One trusts that his famed photographs will be included in any republication of this paper. Dr. von Sallmann's paper on "Hereditary dyskeratosis of the perilimbal conjunctiva" is interesting from both an ophthalmologic and sociologic viewpoint. The group reported is a mixture of Indian, Negro and Caucasian origin called the Halowar Indians. Dr. Woods contributes a delightful discussion on a similar group called the "We-sorts."

Dr. Leopold and his group have found that erythrocyte cholinesterase levels are lower in glaucoma patients than in the normal population. This is the first time that a true systemic organic difference has been demonstrated between these two groups. The fallibility of applying animal data to humans is demonstrated by Dr. L. B. Sheppard. He shows that the rabbit has intrascleral drainage channels and Duke-Elder points out in his discussion that a great many of our conclusions on human drainage channels have been derived from work on rabbits—without an appreciation of the true mechanism for such drainage in this animal. Guerry and Wiesinger report on their experiences with "Light coagulation of fundus lesions." The Bedellism that follows is delightful: "The authors have operated upon three cases which would have been better without light coagulation." Dr. Cogan upholds the "pure" research standard with an article on "Retinal dehydrogenases."

That perennial subject of interest, cataract surgery, is again well represented in this

volume. Dr. Henderson reports a spectacular case of survival of an eye after expulsive hemorrhage. Dr. Calhoun describes the use of a bipronged needle for trapping dislocated lenses; this might be called the whirling patient technique. Dr. Chandler describes a slightly simpler technique. He irrigates the lens out of the vitreous! Furthermore, after one such procedure "the patient was discharged on the fourth postoperative day"! Dr. Thorpe presents almost a monograph on the use of chymotrypsin and the lengthy discussion that follows indicates the timeliness of this subject.

The meetings concluded with two papers on that ever-thorny problem, uveitis. Dr. Alan Woods indicates that histoplasmosis may be a more common etiologic agent than has been thought hitherto, and Dr. Falls continues this thought with a report of the successful treatment of nine such cases with amphotericin B.

The volume closes with seven candidate theses. These are of the usual excellence and of particular interest is the monograph by V. A. Byrnes on ocular injury from high-G forces. These apparently result from increased intravascular pressure. Injuries in a variety of experimental animals are illustrated and the conclusion to be drawn is that, if invited to a ride on a test-slide, stay home.

David Shoch.

YEAR-BOOK OF OPHTHALMOLOGY (1959-1960). Edited by William F. Hughes, M.D. Chicago, The Year-Book Publishers, 1960. 406 pages, 95 illustrations, subject and author indices. Price: $8.00.

A short publisher's note announces that Dr. Derrick Vail has retired as editor after 10 years of faithful service and that this responsibility is now assumed by Dr. William Hughes. In accordance with the policy originally established, the featured overture is the annual special article. This year the opus is "Clinical electroretinography," by Alex E. Krill, who gives a well-rounded, timely presentation with a full bibliography. The intense interest aroused by alpha chymotrypsin is reflected in eight detailed abstracts. After one of his own articles, Hughes notes with wry modesty "No comment!" This annotation is particularly facetious since only one-fourth to one-half of the articles abstracted in the various listings receive any commentary whatsoever. The comments, all of which are interesting, vary from a line or two to almost a page. In a new departure Hughes has delegated some of the commentary to qualified experts. To these annotations the name of the commentator is affixed. The special commentators include Theodore Schwartz on experimental exophthalmos, von Noorden on pleoptic methods, Thygeson on trachoma, Snydacker on gonioscopy, Bernard Becker on tonography and diabetic retinopathy, von Sallmann on experimental cataract, Alan Woods on amphotericin-B, Iser on the electroretinogram, Gibbs on the electroencephalogram, Olwin on anticoagulants, Harrington on visual fields and Walsh on neuro-ophthalmology.

The conscientious ophthalmologist finds as his practice augments that both the need and the difficulty of keeping up with the literature steadily increase. For those so afflicted, the *Year-Book* is an excellent first-aid.

James E. Lebensohn.

JAN EVANGELISTA PURKYNĚ, Czech Scientist and Patriot, 1787-1869. By Henry J. John, M.D. Published as Volume 49 of the *Memoirs* of the American Philosophical Society, September, 1959. Cloth, 94 pages, 26 figures. Price: Not listed.

Most physicians know barely more about Jan Evangelista Purkyně than that his awkward-sounding name is attached to numerous structures and phenomena in medical science. The familiar spelling of his name "Purkinje" is the phonetic German version of the original Czech. In this book Purkyně's life and scientific endeavors are

for the first time comprehensively treated in English. The material was meticulously collected and translated from Czech, Latin, and German sources by Dr. John, who has been for many years a messenger of cultural exchange between his native land, Czechoslovakia, and his adopted country, America. The presentation reveals a subtle treatment of a difficult biographic subject which has brought life near by the warmth of love and admiration for the physiologist Purkyně as one of the greatest men in medical science. Purkyně's discoveries and inventions in medicine were numerous. In many instances he never published descriptions of his innovations. In other cases he gave a cryptic account by pointing out the importance of the principles underlying his discoveries without bothering to follow them up by technical perfections and applications. These he left to others. He founded the first Institute of Physiology of the world at the University of Breslau in 1839, introduced the technique of lecturing with experiment demonstrations, and set up the first medical physiology student laboratory. He laid the foundation of modern histology, discovered the nerve axis cylinder, various types of brain cells, the cilia in the oviduct, the conduction system cells of the ventricle, and described the chick embryo development.

Some of his discoveries are of particular interest to ophthalmologists because they became the basis for modern ophthalmic science. He described, in 1823, the forerunner of the ophthalmoscope and after performing with it the first retinoscopy of the human eye he stated, "Thus by a light property reflected and the careful eye of the observer looking into the eye, no eye membrane or the liquid within the eye will remain hidden. The practitioners who reject the investigations of the physiologist will not refuse to accept this, nor will they be afraid to do it, for they shall find this useful in the diagnosis of eye conditions." Apparently, "They" were afraid to do it. It took about three decades until von Helmholtz took up Purkyně's idea and constructed the ophthalmoscope.

In 1825, Purkyně published the discovery of the so-called Katopric-dioptric pictures, known as Purkyně-Sanson images or reflections of bright objects on the surfaces of the cornea and lens. This created the basis for ophthalmometry. Even Gulstrand's slitlamp and the corneal microscope were derived from Purkyně's earlier device for oblique illumination of the ocular media. In 1830, he developed the "Kinescope" to use so-called "living pictures" for demonstrations of body movements and became thereby a "Walt Disney ancestor." Not only these interesting features of the history of ophthalmology but also a wealth of material concerning Purkyně's histologic and physiologic discoveries are presented in this attractively written and charmingly illustrated book.

Gerhard A. Brecher.

ABSTRACT DEPARTMENT

EDITED BY DR. F. HERBERT HAESSLER

Abstracts are classified under the divisions listed below. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. Anatomy, embryology, and comparative ophthalmology
2. General pathology, bacteriology, immunology
3. Vegetative physiology, biochemistry, pharmacology, toxicology
4. Physiologic optics, refraction, color vision
5. Diagnosis and therapy
6. Ocular motility
7. Conjunctiva, cornea, sclera
8. Uvea, sympathetic disease, aqueous
9. Glaucoma and ocular tension
10. Crystalline lens
11. Retina and vitreous
12. Optic nerve and chiasm
13. Neuro-ophthalmology
14. Eyeball, orbit, sinuses
15. Eyelids, lacrimal apparatus
16. Tumors
17. Injuries
18. Systemic disease and parasites
19. Congenital deformities, heredity
20. Hygiene, sociology, education, and history

6
OCULAR MOTILITY

Saiduzzafar, H. **Variant of Duane's retraction syndrome.** Brit. J. Ophth. **43**: 700-702, Nov., 1959.

Duane's retraction syndrome is a not uncommon congenital abnormality of the horizontal eye muscles, most commonly the external rectus muscle of one eye, and is not associated with any lesion of the central nervous system. Usually there is limitation or absence of abduction and retraction of the globe on attempted adduction. It is felt by most observers that this is due to a replacement of the muscle by an inelastic fibrous band which can neither contract nor relax so that on adduction the eye simply is retracted backwards instead of moving inwards. Diplopia is usually absent since the condition is present from birth.

The case of a 16-year-old girl is described who had the typical picture of the disease with the added features of diplopia, head tilting, and difficulty of adduction. (4 figures, 3 references)

Morris Kaplan.

Stanworth, A. and DaCunha, D. **Binocular mechanisms in small-angle strabismus.** Brit. J. Ophth. **43**:648-661, Nov., 1959.

In many cases of strabismus it is quite possible to eliminate the angle of deviation and to bring about binocular vision but this is not always possible even in patients who show strong fusion and stereopsis. In these latter there may be abnormal retinal correspondence even though the angle of deviation is minute. Thus it is quite possible that patients who seem to have had their squints cured are left with small-angle strabismus due to fixation disparity. It is also possible that at clinical examination these eyes present binocular vision while in everyday usage the patient is indeed suppressing.

A number of cases are described to illustrate the various binocular mechanisms and disparities which are to be found in everyday use of the eyes. These include subjects with normal as well as with abnormal retinal correspondence and other combinations of fixation disparities. The distinctions between these various abnormalities in small-angle strabismus may be very indefinite. (9 references)

Morris Kaplan.

7
CONJUNCTIVA, CORNEA, SCLERA

Bietti, G. B. and Ferraboschi, G. **A statistical analysis of the association of keratoconus with vernal conjunctivitis.** Boll. d'ocul. **38**:85-102, 1959.

In an effort to determine if there were more than a casual association between keratoconus and vernal conjunctivitis the authors reviewed the clinical records of 199,300 outpatients over the age of nine years. In this series the authors found 733 cases of vernal conjunctivitis and 182 cases of keratoconus and in ten of the patients both of the conditions existed. This suggests association between the two conditions. The authors do not consider keratoconus a consequence of vernal catarrh, but feel that there may be a common constitutional background in both of these conditions. (13 figures, 55 references) Joseph E. Alfano.

Castroviejo, Ramon. **Plastic and reconstructive surgery of the conjunctiva.** Plast. & Reconstruct. Surg. **24**:1-12, July, 1959.

The author describes his procedures. (13 figures) F. H. Haessler.

Lindner, K. **The etiology of bacterial infectious inflammations of the conjunctiva.** Arch. f. Ophth. **161**:309-318, 1959.

In this lecture on the inflammations of the conjunctiva which can be ascribed to bacterial infection the author gives a useful general summary but, as he says, offers nothing fundamentally new. Endemics of bacterial conjunctivitis have disappeared and isolated instances are uncommon. Just this circumstance makes it possible now to investigate the role of the questionable causative organisms which are ever present. For example one could study the importance of staphylococcus in infectious conjunctivitis or of Bacterium coli in the now uncommon blennorrhia of the newborn and one would rarely be disturbed by gonococcus or inclusion virus because both have all but disappeared. Bacterium coli is still amply present in every delivery. (2 figures, 27 references) F. H. Haessler.

Vancea, P., Vaighel, V. and Vancea, P. P. **Trophic ulcer of the cornea following operations on the ocular muscles,** Ann. d'ocul. **193**:28-34, Jan., 1960.

Five cases are reported in which limbal ulcers developed eight to 14 days after extraocular surgery. In each case a bilateral advancement of the lateral recti was done. The authors feel that the etiologic factor is the interference with the nutrition of the cornea as a result of sectioning limbal vessels. However, they point out that, under these circumstances trophic ulcers should be seen more often. In the cases here described the lesion healed uneventfully. (15 references) David Shoch.

8
UVEA, SYMPATHETIC DISEASE, AQUEOUS

Ruiz Barranco, F. **The participation of the meninges in uveitis.** Arch. Soc. oftal. hispano-am. **19**:786-795, Oct., 1959.

To determine the relationship between the involvement of the uvea and the meninges, the cerebrospinal fluid of 100 patients with nontraumatic uveitis was examined for sodium, glucose, protein, cells, bacteria, Wasserman reaction, and colloidal gold curve. In 99 cases the fluid was clear. The sodium content was diminished in 60 cases, normal in 30 and increased in 10. Albumen was increased slightly in 15 cases, and significantly in 20. Globulins were slightly positive in 15, positive in seven, and strongly positive in six. The cells were normal in 37, slightly increased in 32, and definitely increased in 31 cases. No bacteria were found. The Wasserman reaction was positive in 15 cases, and the colloidal curve was abnormal in 20. The meninges were thus nor-

mal in 37 cases, slightly involved in 32, and definitely involved in 31. The author finds frequent participation of the meninges in recurrent uveitis and in luetic and viral uveitis. The meninges participate rarely in uveitis of tuberculous and local origin. The clinical implication of this study is the necessity of general therapy in uveitis which simultaneously involves the meninges. (2 tables, 7 references) Ray K. Daily.

9

GLAUCOMA AND OCULAR TENSION

Diaz Dominguez, D. and Ruiz Barranco, F. **A contribution to tonographic calculations.** Arch. Soc. oftal. hispano-am. **19**:773-785, Oct., 1959.

The authors failed to verify Leydhecker's tonographic data. Their study consisted of tonography lasting ten minutes and an analysis of the tonographic curve in three parts, namely that of the first four minutes, of the next three minutes and of the last three. They conclude that the first three minutes are of great importance, and these data should be included in the calculations. From a diagnostic standpoint the authors found it advantageous to extend the tonography to ten minutes. In their calculations Leydhecker's index for doubtful cases was not reliable, and they found no diagnostic value in the relation of Po/C. (4 tables, 12 references) Ray K. Daily.

Epstein, E. **Fibrosing response to aqueous. Its relation to glaucoma.** Brit. J. Ophth. **43**:641-647, Nov., 1959.

The keloid tendencies of the African races makes glaucoma surgery in these patients particularly difficult and seemingly automatically condemns the operation to failure. To obviate this danger, a procedure of introducing a very fine polyethylene tube into the anterior chamber and extending as a loose end beneath the conjunctiva was elaborated. This functioned very well for a short time but invariably the distal end became clogged; it was determined that the aqueous fluid had a fibrosing influence on the subconjunctival tissue. It is probable that this end result does not usually occur in the usual filtering procedures because there is some epitheliazation of the bleb cells. As an alternative procedure a paralimbal lamellar sclerotomy was performed so as to permit free communication between severed aqueous veins and the subconjunctival spaces. This precedure has functioned very well in several cases over several months and it is suggested that it be considered further. (5 figures)

Morris Kaplan.

Foulds, W. **Darkroom outflow test in unilateral closed-angle glaucoma.** Brit. J. Ophth. **43**:697-699, Nov., 1959.

It has long been noted that when one eye has closed-angle glaucoma, the fellow eye is most likely to become similarly affected in time; this has been borne out by numerous tests and clinical studies. The dark room outflow test has been found to be quite sensitive and with it apparently unilateral closed-angle glaucoma was investigated in 79 patients; 17 of these had had symptoms in the fellow eye and 62 were free from symptoms. A positive rise of over 8 mm. Hg was found in 22 of the 79 and a marked decrease in the facility of aqueous outflow was found in 45. Foulds suggests that the dark room test should be done in all cases of unilateral closed-angle glaucoma and it is suggested that a prophylactic peripheral iridectomy be done on the fellow eye, especially if this eye is anatomically similar to the affected one. (8 references)

Morris Kaplan.

Leydhecker, W. **Nervous influences on the intraocular pressure.** Arch. f. Ophth. **161**:362-372, 1959.

Influences of the central nervous system per se do not bring about glaucoma. No cerebral disturbance is known which is constantly accompanied by glaucoma and there is no glaucoma which is regularly associated with cerebral, somatic, or mental disturbance. On the other hand, many local disturbances in the eye are known to be associated with glaucoma, and central nervous disturbances which may raise the tension only slightly in the normal bring about greater changes in the glaucomatous eye. (73 references)

F. H. Haessler.

Nordmann, J. **Certain fundamental questions concerning glaucoma.** Ann. d'ocul. **193**:17-27, Jan., 1960.

This is the second part of a two-part article on glaucoma. The first, which appeared in 1959, dealt with the question of the central origin of glaucoma. The author concluded that there was no evidence to justify such a hypothesis and that, at this time, glaucoma must be considered primarily a disease of the eye.

In this second article he discusses the question as to whether ocular hypertension is a fundamental element of glaucoma. Hypertension in relation to excavation of the optic nerve and field defects is discussed and the author comes to the conclusion that the primary factor in glaucoma is the ocular hypertension. Two special cases are considered: hypertension without glaucoma and glaucoma without hypertension. He feels that the first group consists of those who have not yet demonstrated glaucomatous defects but will in time, and that in the second group ocular hypertension may have been present in the past but is now compensated by a diminution in aqueous flow. In these cases there frequently is a positive response to provocative tests. (34 references)

David Shoch.

Vanni, V. and Lepri, L. **A clinical study of the influence of hyaluronidase on the intraocular pressure.** Boll. d'ocul. **38**: 114-132, 1959.

The authors studied the action of hyaluronidase on the intraocular pressure of normal and glaucomatous eyes after introducing hyaluronidase into the eye by iontophoresis. The results were quite uniform and reliable in spite of some of the difficulties of the technique. There was no lowering of the intraocular pressure or change in the tonometric curve in their cases of angle-closure glaucoma or in glaucoma secondary to dislocation of the lens. The results in open-angle glaucoma were quite remarkable, there being a marked lowering of the intraocular pressure. The degree of lowering of the intraocular pressure was greatest where the initial pressure was the highest. The effect lasted from one to three days. (3 tables, 50 references)

Joseph E. Alfano.

10
CRYSTALLINE LENS

Jenkins, B. **The use of alpha-chymotrypsin in cataract surgery.** South. M. J. **53**:44-46, Jan., 1960.

The author describes his discovery in 1955 of the zonulytic properties of alpha-chymotrypsin, which resulted from a fortuitous observation while using the enzyme in an attempt to dissolve vitreous opacities. Two months later a 1:1000 solution of the enzyme was successfully used in a cataract extraction and found to facilitate the procedure without causing adverse effects. His subsequent experience in 127 cataract extractions with enzymatic zonulysis have convinced him of the efficacy and safety of this technique. In the author's technique a 1:5000 solution of the enzyme is injected into the posterior chamber through a blunt cannula. He waits two to four minutes for zonulysis to occur, during which time an iridectomy is performed if desired. The

lens is delivered with a mechanical erisophake by sliding. The anterior chamber is then lavaged with normal saline to remove remaining traces of enzyme. The author reports that he and Raiford have used the enzyme successfully in 26 cases of cataract extraction in children under 15 years of age, and in his opinion the instances of vitreous loss reported by others in this age group require clarification, since they are not necessarily a result of using the enzyme. (6 references) Joseph H. Derivaux.

Martins, M. **Preoperative treatment of patients with cataract.** Rev. brasil. oftal. **18**:343-347, Dec., 1959.

The author advises that before operation patients with cataract be given complete eye examinations with slitlamp biomicroscopy, gonioscopy, tonometry, keratometry and at times, tonographic studies. He advises bacterial studies of conjunctival secretions only when there is some congestion. Irrigations of the lacrimal system have been abandoned. A general physical examination, including blood count and urinalysis, is also done. The patient receives a collyrium containing a sulfa drug for a few days before surgery and also a broad-spectrum antibiotic. Walter Mayer.

Nørskow, K. **Comparison of 50 cataract operations with and 50 without the aid of alpha-chymotrypsin.** Acta ophth. **37**:546-551, 1959.

Alpha-chymotrypsin facilitated the operation, raised the number of intracapsular operations from 37 to 47, and no postoperative complications were observed. (28 references) John J. Stern.

Svane-Knudsen, P. **Severe secondary ocular changes in a patient with idiopathic hypoparathyroidism and pernicious anaemia.** Acta ophth. **37**:560-567, 1959.

A female patient, aged 45 years, had had idiopathic hypoparathyroidism with convulsions since the age of seven years. At the age of 11 to 12 years, bilateral zonular cataracts started to develop; at the age of 18 years bilateral discission was undertaken. A hemorrhage in the left eye destroyed useful vision but the operation in the other eye was successful. Eight years later attacks of severe keratitis started which resulted in corneal scars with chalk deposits. Twenty-two years after the unsuccessful cataract operation the right eye developed glaucoma which responded to local treatment; at the age of 43 years cyclodialysis was undertaken. Because of the corneal scars a corneal transplantation was done in the left eye which resulted in glaucoma, and a decompression operation was followed by a massive hemorrhage. The transplant became opaque and sight was lost. (20 references) John J. Stern.

11
RETINA AND VITREOUS

Bauer, F. **A case of Coats' retinitis exudativa externa with attention to histologic changes.** Arch. f. Ophth. **161**:373-380, 1959.

Bauer noted changes originating in the vascular system, such as edema, exudation, hemorrhage and cellular infiltration; proliferative processes in glial tissue, degenerative changes in the retinal elements, the vessels, and in newly-formed glial tissue, and pigmentation. The newly-formed glial tissue showed phagocytic activity. (9 figures, 21 references) F. H. Haessler.

Behrendt, T. **Fundus changes in hypertensive diseases.** Rev. brasil. oftal. **18**: 305-309, Dec., 1959.

The author compares the advantages of black and white and of color photography in the evaluation of fundus changes in hypertension. He finds that black-and-white photography is preferable for the

vessel wall and its changes, for small vessels and for exudates and edema; color photography is preferable for a general view, for hemorrhages and when color is an important factor for diagnosis. (2 figures) Walter Mayer.

Larsen, H. W. **X-ray therapy in proliferative diabetic retinopathy.** Acta ophth. **37**:531-536, 1959.

In 50 patients with proliferative diabetic retinopathy who were given X-ray treatment of the posterior segment (200 r (air) for five to 15 consecutive days) no improvement was noted. (3 figures, 5 references) John J. Stern.

12
OPTIC NERVE AND CHIASM

Gjessing, H. G. A. **Pits or crater-like holes in the optic disc.** Acta ophth. **37**: 528-530, 1959.

The literature is reviewed briefly and a case of a deep, crater-like pit in the disc of one eye without disturbance of the function is described. (1 figure) John J. Stern.

Vedel-Jensen, N. **Optic tract neuritis in multiple sclerosis.** Acta ophth. **37**:537-545, 1959.

The literature is reviewed and two cases of multiple sclerosis are presented in which there were homonymous hemianopic field defects without macular sparing. The lesion must be lying somewhere behind the optic chiasma. (2 figures, 14 references) John J. Stern.

Zülch, K. J. and Nover, A. **The spongioblastomas of the optic nerve.** Arch. f. Ophth. **161**:405-419, 1960.

The primary tumors which arise in the glia of the optic nerve are usually referred to as gliomas in the ophthalmologic literature but there are differences of opinion at to the more precise details in the system of the gliomas. The authors report details of microscopic structure in 29 cases. Attention was given to architecture, regressive manifestations, infiltration of the arachnoid sheath and connective tissue septa as well as to the behavior of ground substance of the fasciculus opticus. In the biologic characterization attention was given to age, sexual distribution, the slight malignancy and the rate of growth. Postoperative survival as great as 10 years was noted and among 16 patients operated upon there was only one recurrence.

Many similarities were noted in morphology and clinical behavior of these tumors and the spongioblastomas of the central nervous system which leads the authors to suggest that these neoplasms be referred to as spongioblastomas. (12 figures, 42 references) F. H. Haessler.

13
NEURO-OPHTHALMOLOGY

Fanta, H. **The visual field for movement and white objects with intracranial processes.** Arch. f. Ophth. **161**:492-501, 1960.

The difference between the visual field for a moving white target and for white as a color is easily recognized and registered in intracranial processes, particularly in lesions which occupy space. Comparative studies with quantitative perimetry confirm the usefulness of such results. The contraction of the field can probably be ascribed to the increased pressure which is a result of the occupation of space. With direct injury to the optic nerve or tract this discrepancy was not so striking. (11 figures, 10 references) F. H. Haessler.

Leoz, Gustavo. **Homonymous hemianopsias.** Arch. Soc. oftal. hispano-am. **19**:563-771, Aug. and Sept., 1959.

This is an exhaustive monograph on

the subject of homonymous hemianopsia. The first part reviews the antomy and symytoms of lesions of the visual pathways, and the various methods of perimetric examination. The author's preference is for the Goldmann perimeter, which was used for the examination of his material, comprising 183 cases. The Bjerrum screen was used in addition for the examination of the central field. With the Goldmann perimeter the author used test discs 1 mm. and 0.25 mm. in diameter and illumination of 1.00 and 0.096 for the examination of the central and median isopters. Thirty cases are reported in detail, illustrated with roentgenograms and visual fields. The reported cases comprise tumors of the hypophysis, of the diencephalon, temporal lobe, cerebellum, intracerebral hematoma, hematoma of the parietal lobe, cyst of the temporal lobe, Meniere's disease associated with visual loss, disseminated encephalitis, vascular malformations in the parietal and temporal regions, aneurysm of the choroid plexus, and hemianopsias following chemical or thermal pallidectomies, and hemispherectomies. Homonymous hemianopsia is the perimetric manifestation of a retrochiasmatic lesion of the optic pathway. The therapy of such lesions is not within the sphere of the ophthalmologist, but the precision of the perimetric examination is important in the localization of the lesion. The author refutes the general impression that lesions of the optic pathway always produce incongruent hemianopsia, while lesions of the optic radiation produce congruent defects. He emphasizes that congruence of the visual field defect depends more on the type of the lesion than on its localization. Vascular lesions of the optic pathways always produce congruent defects. Their localization requires additional data derived from such tests as the Wenicke pupillary reaction, the search for descending optic atrophy, arteriography, ventriculography, and electroencephalograms. Expending lesions, infectious or traumatic, but not of vascular origin, present initially incongruent manifestations regardless of their localization. Only when the lesions have progressed, do retrogeniculate lesions give rise to congruent defects of the visual field, while lesions anterior to the geniculate bodies produce incongruent defects. The author does not believe that with our present means of clinical examination it is possible to determine whether the macula has or has not been spared, because it is impossible to be certain that the patient is not using extrafoveal fixation during the examination. It is pointed out that so far there is no anatomic basis for the assumption of the existence of bilateral macular representation. There is also no conclusive evidence that the geniculate bodies have a connection with the contralateral visual cortex. The persistance of good central visual acuity in lesions of the occipital lobe may be due to various factors; one of these is the extensive representation of the macular region in the occipital cortex, and another is the constant physiologic change in fixation. The author believes that it is possible for the lower visual centers to acquire a certain degree of visual perception, as has been demonstrated in monkeys. (163 figures, 45 references) Ray K. Daily.

Sanchez-Salorio, M. and Molina Negro, P. **Unilateral and atypical Argyll Robertson pupil.** Arch. Soc. oftal. hispano-am. 19:786-804, Oct., 1959.

This is a detailed report of a clinical case, of a girl 17 years old, who was hospitalized for headaches, vomiting and nausea. She was found to have an anisocoria, the left pupil being slightly larger. The pupillary reactions were normal in the right eye. In the left eye the reaction to light was at first delayed; on repetition of the test it became abolished,

and on further stimulation there was paradoxic pupillary dilatation. There was no psychosensorial response of the pupil to sticking a pin in the arm. The patient refused surgery, and as the symptoms became aggravated she passed into coma; at this time she developed bilateral papilledema. On postmortem the diagnosis of a mesencephalic tumor involving the aqueduct and the third ventricle was confirmed. (10 figures) Ray K. Daily.

16
TUMORS

Jensen, O. A. and Andersen, S. R. **Late complications of biopsy in intraocular tumors.** Acta ophth. **37**:568-575, 1959.

Intraocular biopsy was done in five eyes with benign lesions, in one with retinoblastoma and in 17 with malignant melanomas. Of the 17 patients, 10 had died from metastases one to five years after biopsy, and of the seven survivors after five to eight years, only four had no orbital recurrence or metastases. The number of orbital recurrences was larger than expected and the method is to be regarded as too dangerous for a routine procedure. (4 figures, 6 references)
John J. Stern.

Maione, Mario. **The origin of the cellular elements and on the mechanism of diffusion of blastomes of the retina.** Ann. d'ocul. **192**:897-918, Dec. 1959.

The histopathology of an eye with retinoblastoma is described and additional eyes in the author's laboratory are reviewed. From these studies he concludes that there are two phases in the development of retinoblastoma. First, there is a generalized disorder of retinal development so that all types of retinal cells may be seen in all stages of development. Secondarily, a true neoplastic change occurs with wild growth of cells in one or more areas. In essence he feels that a retinoblastoma develops only in a previously disordered retina. (22 references, 13 figures) David Shoch.

17
INJURIES

Flynn, J. A. F. **Watching an eclipse of the sun.** M. J. Australia **1**:85-87, 1960.

One hundred and seventy Australians, mainly school children, suffered impaired vision from watching a solar eclipse on April 8, 1959. The author describes various pinhole projection methods whereby an eclipse of the sun can be viewed indirectly and safely. Ronald Lowe.

Grönvall, H. and Hultgren, A. **Ocular splinters of steel, some clinical and metallographic data.** Acta ophth. **37**:413-466, 1959.

Steel splinters extracted from 103 eyes during a 20-year period were examined metallurgically and some clinical observations are reviewed. In 131 cases the splinter was located in the eye. Most splinters came from a hammer and all had been extracted with a magnet. The smallest weighed 0.1 mg., the smallest one from the posterior segment 0.4 mg., five weighed more than 0.1 gm. and one of them as much as 12.3 gm. Splinters from the right eye are more numerous in the lower weight groups; in the left eye heavier splinters were predominant. Some of the tools used were examined metallographically, and the findings were compared with those of 19 selected cases of intraocular foreign bodies. Plastic deformation of hardened and unhardened steel, cracking and splintering of steel were investigated. The article is illustrated profusely with metallurgical micrographs. (28 figures) John J. Stern.

18
SYSTEMIC DISEASE AND PARASITES

Fatorelli, A. **Ocular histoplasmosis.** Rev. brasil. oftal. **18**:349-359, Dec., 1959.

The author reviews the knowledge available about ocular histoplasmosis and describes a case of uveitis in which this etiologic factor was suspected. (15 references) Walter Mayer.

Kornerup, T. and Lodin, A. **Ocular changes in 100 cases of Besnier's prurigo (atopic dermatitis).** Acta ophth. **37**:508-521, 1959.

In 100 cases of atopic dermatitis, only three showed a mild degree of lenticular involvement, mostly a thin posterior subcapsular opacity. This low incidence of cataractous changes as compared with that reported by others may be accounted for by the narrower definition of the skin disease. No keratoconus was observed and low-grade "bi-oblique astigmatism" was more frequent among the cases of dermatitis than among the controls. (4 figures, 36 references) John J. Stern.

Mueller, F. **Acquired ocular toxoplasmosis.** Arch. f. Ophth. **161**:341-361, 1959.

The occurrence of acquired ocular toxoplasmosis has been recognized only recently and in a few cases. It can be established only after enucleation of the eye; the serological findings are merely a symptom. The author took blood for the determination of the SFT from all patients in whom an eye had to be enucleated and used one-half of the eyeball for animal experimentation. The diagnoses in 103 enculeated eyes were chiefly injury, tumor, inflammation, and glaucoma. In two cases toxoplasma was demonstrable in animal experiments. In one of them it was a congenital toxoplasmosis where a positive result was to be expected. In the other patient retinal glioma was found in both eyes. In both eyes the causative agent was found. The second eye was enucleated four years after the first. Histologic examination revealed intra- and extracellular granular calcification which was ascribed to a toxoplasmosis which was probably a congenital latent one. In a third patient a generalized and probably acquired toxoplasmosis was found. Five days before death the fundus was normal in each eye, and post mortem organisms were demonstrable by animal inoculation. No histologic abnormalities were demonstrable. In the two patients with congenital toxoplasmosis the SFT was negative although it was positive in 60 percent of the 103 cases. In only one patient, who had glioma, were toxoplasma organisms unexpectedly found. In 12 cases of retinouveitis, where a positive reaction was to be expected, this occurred only once. (4 figures, 4 tables, 73 references) F. H. Haessler.

Rodger, F. C. and Farooqui, H. U. **Lesions of the lid margins caused by ectoparasites in India.** Brit. J. Ophth. **43**:676-680, Nov., 1959.

Infestation of the lid margins with ectoparasites is very common in India and results in considerable discomfort with secondary inflammation and abscesses of the lids and eyebrows brought on by the scratching of the areas. The infestation is by either the head or body louse or even frequently by the public louse and also by the follicular mites which are obtained from the dog. The appearance of the disease is often similar to trachoma. (2 figures, 17 references) Morris Kaplan.

19
CONGENITAL DEFORMITIES, HEREDITY

Magnussen, K. **Hereditary isolated ocular albinism with pendular movement of the head in rabbits compared with comparable anomalies in man.** Arch f. Ophth. **161**:502-518, 1960.

A recessive mutation in a rabbit gave rise to an isolated albinism of the eye which corresponds to an eye-limited human albinism. The latter was, however, inherited as a gonosomal recessive trait.

Both mutations produce suppression of pigmentation of the ocular ectoderm whereas there is greater variation in the mesodermal tissues. Decreased vision was noted in both man and animals. The nystagmus which is constant in man was also noted in some of the rabbits. Aside from a close functional association between the eye and the vestibular apparatus, the ontogenesis of these organs suggests the possibility of the action of one gene on both organs. (6 figures, 38 references)

F. H. Haessler.

20
HYGIENE, SOCIOLOGY, EDUCATION, AND HISTORY

Bejat, M. **Mortality in ophthalmology.** Ann. d'ocul. **192**:919-933, Dec., 1959.

Between 1942 and 1958 there were 23 deaths in a total of 15,786 patients in three large eye services in Paris. The author divides these into five groups. In Group I four patients (one in 4,000) died of neoplastic disease of which the eye was a part; for example metastatic lung and stomach cancers. In Group II four patients died of virulent infections of the orbital region. In Group III three patients died before any surgery, one of pneumonia and two of vascular accidents. In Group IV—anesthetic deaths—two children, aged 11, died of general anesthesia of a total of 2,162 general anesthetics given for a rate of 1/1000. No deaths were referable to local anesthesia.

Group V—post operative deaths—ten deaths occured in 17,036 patients operated upon, or about 1/2000. Two of the deaths followed antiglaucoma procedures, five cataract extractions, and three followed repair of retinal detachment. Almost all of the deaths occurred in aged people and were ascribed to a vascular disturbance. The author advises monocular dressings, early ambulation, massage, and breathing exercises to minimize the mortality in this group. (20 references)

David Shoch.

Theobalt, L. **What occupations are open to the young blind?** Ann. d'ocul. **193**:35-56, Jan., 1960.

The author discusses the public treatment of the blind across the ages. He covers the Orient, the near East and Europe. Fascinating vignettes on notable blind people are given, and the first section closes with a discussion of the development of Braille notation.

In the second section he discusses the psychology and education of the blind and reviews the occupations of 120 graduates of the "National Institute of the Young Blind" in Paris. Of 120 such graduates 55 are either musicians or piano tuners. Significant is the fact that in the entire group only 37 (about one-third) were satisfied with their occupations. The author feels that this can be remedied by opening more occupations to the blind and by beginning to train the young blind for useful occupations at an early age. This demands an understanding public that will open more lines of endeavor to the blind. (21 references)

David Shoch.

NEWS ITEMS

EDITED BY DONALD J. LYLE, M.D.
411 Oak Street, Cincinnati 19, Ohio

News items should reach the editor by the 10th of the month. For adequate publicity, notice of postgraduate courses and meetings should be received three months in advance.

DEATHS

Dr. Delamere Forest Harbridge, Phoenix, Arizona, died October 6, 1959, aged 87 years.

Dr. Donald Hunter O'Rourke, Denver, Colorado, died December 27, 1959, aged 66 years.

Dr. William Campbell Posey, Jr., Bryn Mawr, Pennsylvania, died January 2, 1960, aged 45 years.

ANNOUNCEMENTS

FITTING CONTACT LENSES

The University of Texas Postgraduate School of Medicine announces a course in theory and practical fitting of contact lenses to be held in Houston, Texas on May 23, 24, 25, and 26, 1960.

The instructors for this course will be ophthalmologists who are experienced in the fitting of contact lenses. This course is designed so that those completing it will be proficient in all phases of contact lens fitting and adjusting. The course is limited to 20 physicians certified by the American Board of Ophthalmology.

For further information write:

Office of the Dean, The University of Texas Postgraduate School of Medicine, 410 Jesse Jones Library Building, Texas Medical Center, Houston 25, Texas.

ORTHOPTIC EXAMINATIONS

The annual examination of orthoptic technicians by the American Orthoptic Council will be conducted in August and October, 1960.

The written examination will be nonassembled and will take place on Thursday, August 18th, in certain assigned cities and will be proctored by designated ophthalmologists.

The oral and practical examinations will be on Saturday, October 8th, in Chicago, just preceding the meeting of the American Academy of Ophthalmology and Otolaryngology.

Application for examination will be received by the office of the chairman of examinations, Dr. Frank D. Costenbader, 1605 22nd Street, N.W., Washington 8, D.C., and must be accompanied by the examination fee of $30.00. Applications will not be accepted after July 1, 1960.

PROGRAM SECTION ON OPHTHALMOLOGY

On the program for the Section on Ophthalmology, American Medical Association, meeting at the Eden Roc Hotel, Miami Beach, Florida, on the afternoons of June 14th, 15th, and 16th are:

Tuesday, June 14th, at 1:30 P.M.: "The selection of operative procedures in vertical muscle imbalances," Edward A. Dunlap, New York; "Vertical recti transplanatation in the A and V-syndromes," James E. Miller, Saint Louis; (Panel discussion by Philip Knapp, New York, and Charles F. Cooper, Jr., Atlanta).

"Ultrasonography: An aid in orbital tumor diagnosis," Gilbert Baum, Bronx, (Discussion to be opened by Elmer J. Ballintine, Cleveland); "Granuloma as a complication of polyethylene tube buckling procedures for retinal detachment," Harvey Lincoff, New York, (Discussion to be opened by Silvio von Pirquet, Boston); "Precancerous epithelioma of the limbus," Frank C. Winter, and Thomas R. Kleh, Palo Alto, (Discussion to be opened by John S. McGavic, Bryn Mawr); "Pathology of ocular leprosy: I. Cornea," James H. Allen, New Orleans, and Jerome L. Byers, Dallas, (Discussion to be opened by D. P. Choyce, London, England); "Electroretinography in pediatric ophthalmology," George Goodman, and Harris Ripps, Ph.D., New York, (Discussion to be opened by Hermann M. Burian, Iowa City); "A study of pulseless disease," Joseph L. Dowling, Jr., Providence, and Taylor R. Smith, Boston, (Discussion to be opened by Victor Curtin, Miami).

On Wednesday, June 15th, at 1:30 P.M.: Executive session. "Visual field changes following temporal lobectomy," John Wendland, and Sidney Nerenberg, Minneapolis, (Discussion to be opened by C. Wilbur Rucker, Rochester, Minnesota); "Opsoclonus," J. Lawton Smith, Baltimore, (Discussion to be opened by Edward W. D. Norton, Miami); "Contact lenses for aphakics," Robert C. Welsh, Miami; "Acute complications from modern corneal contact lenses: A report of 14 new cases," Richard K. Lansche, and Robert Lee, Munich, (Discussion to be opened by Elizabeth Constantine, New York); "Recent experiences with light coagulation," Herbert Wiesinger, Walter Geeraets, and DuPont Guerry, III, Richmond, (Panel discussion by William H. Havener, Columbus, and Taylor R. Smith, Boston).

On Thursday, June 16th, at 1:30 P.M., "Recent advances in ocular surgery," will be the theme of the program: "Chairman's Address," Harold G. Scheie, Philadelphia; Address of guest of honor—"Enzymatic zonulolysis in lens extraction," Joaquin Barraquer, Barcelona, Spain, (Discussion to be opened by Derrick T. Vail, Chicago); Address of invited foreign guest: "Anterior chamber lenses: Present operative technique," Benedetto Strampelli, Rome, Italy; Address of invited foreign guest: "Uses of anterior

chamber implants in ocular surgery," D. P. Choyce, London, England, (Panel discussion by Joaquin Barraquer, Barcelona, Spain, and DuPont Guerry, III, Richmond, Virginia); "Surgical treatment of bullous keratopathy," Trygve Gundersen, Boston, (Discussion to be opened by A. Edward Maumenee, Baltimore); "Surgical treatment of epithelial cysts of the anterior chamber," Ernest K. Goodner, and Michael J. Hogan, San Francisco, (Discussion to be opened by Paul A. Chandler, Boston); A report on 42 cases of glaucoma treated by peripheral iridectomy with scleral cautery," George S. Tyner, Duane Lahey, John Elliff, and Harry Watts, Denver, (Panel discussion by John M. McLean, New York and Carteret Lawrence, Baltimore).

Postgraduate courses

The Institute of Ophthalmology of the Americas announces its third series of postgraduate courses for specialists in ophthalmology to be given from September 12th through November 23rd.

Among the courses to be offered are: Advances in ocular prostheses; anomalies of extraocular muscles, including ptosis; biomicroscopy; biomicroscopy using near ultraviolet, cobalt blue and polarized light; clinical bacteriology; clinical problems of tear formation; complications of ophthalmologic surgery; contact lenses; electrophysiology and applied physiology of the eye; enucleation and evisceration; glaucoma; gonioscopy and tonography; keratectomies and keratoplasties; lacrimal-sac surgery; light coagulation (Meyer-Schwickerath apparatus); low-vision aids; ocular biochemistry; ocular geriatrics; ocular microbiology; ocular neuro-ophthalmology; ocular photography; ocular radiology; ocular therapeutics; ophthalmoscopy; orthoptics; pathology; perimetry; physiologic optics; plastic eye surgery; pleoptics and macular function testing; psychosomatic factors in ophthalmology; radioisotopes in ophthalmology; recent advances in cataract surgery; refraction; retinal detachment; surgery of the orbit; and uveitis.

Catalogues and additional information may be obtained by writing to Mrs. Tamar Weber, Registrar, Institute of Ophthalmology of the Americas, New York Eye and Ear Infirmary, 218 Second Avenue, New York 3, New York.

Strabismus course

The Presbyterian Hospital and Medical Center of San Francisco (formerly Stanfard Hospital in San Francisco) presents its second strabismus course, July 13th, 14th, and 15th. The guest lecturer will be Dr. Harold Brown of New York. The other members of the faculty will be Dr. Arthur Jampolsky and Dr. Edward Tamler of San Francisco. Registration fee, $75.00; enrollment limited. For registration or further information contact Secretary, Eye-Bank, 2018 Webster Street, San Francisco 15, California.

Glaucoma course

A one-week course in glaucoma will be given at the Massachusetts Eye and Ear Infirmary under the direction of Dr. Paul A. Chandler, June 6th through June 11th. Topics to be considered will be: Ocular hydrodynamics; gonioscopy, tonography, and perimetry; diagnosis, medical and surgical management. Patients will be available for demonstration and examination. Admission will be limited to 12 persons. Fee: $100.

Application may be made to: Charles Snyder, Registrar, Massachusetts Eye and Ear Infirmary. 243 Charles Street, Boston 14, Massachusetts.

Postgraduate training program

Supported by a grant from the National Institutes of Health, the Departments of Physiology, Ophthalmology, Otolaryngology and Psychology of The University of Michigan join in offering postgraduate training to qualified individuals desiring further research and teaching experience to prepare themselves for independent careers in science.

The emphasis of the program is upon the physiology of sensation, broadly approached through neurophysiology, neuroanatomy, psychophysics and studies of animal behavior. Trainees are encouraged both to develop experimental approaches of their own and to work with a senior staff member on experiments already in progress. Present staff and interests are as follows:

Mathew Alpern, Ph.D., associate professor of ophthalmology, psychology and physiology: Neural factors associated with brightness alterations induced between spatially contiguous stimuli, comparison of photoreception producing pupillomotor responses with that producing subjective visual responses; psychophysiologic studies of patients with ocular abnormalities; mechanisms and interaction of accommodation and convergence; effects of drugs upon retinal processes.

Robert W. Doty, Ph.D., associate professor of physiology: Electrophysiological and behavioral analysis of visual system in cat and monkey with particular reference to role of retino-cortical topographic projection as basis for pattern discrimination; ability of monkeys to differentiate location and temporal pattern of electrical stimulation applied to "sensory," "motor" and "association" cortex and subcortical nuclei, using this stimulation to elicit conditioned reflexes; study of the neural organization of complex stereotyped behavior such as reflex deglutition.

Merle Lawrence, Ph.D., professor of otolaryngology, psychology and physiology: Electrophysiology of the cochlea; normal and pathologic physiology of the inner ear together with histology of the temporal bone; behavioral studies of hearing in animals; psychophysical studies of hearing in human normal and pathologic ears.

In addition to research endeavors and part-time teaching of physiology, trainees may take any or all of the following special courses: "Electronic instrumentation in the biological sciences," K. E. Bignall; "Advanced laboratory in sensory physiology," staff; "Advanced neurophysiology," R. W. Doty; "Physiology of vision," M. Alpern; "Theories of hearing," M. Lawrence; "Sound conduction in the ear," M.

Lawrence; "Developmental and microscopic anatomy of the temporal bone," M. Lawrence.

Trainees must have an M.D. or Ph.D. degree or equivalent, an enduring interest in research, and an outstanding record of scholastic and intellectual attainment. United States citizens or those who have filed a declaration of intent are eligible for training stipends at the following rates, of which $300.00 per month for a total of 36 months is customarily considered tax exempt. Yearly stipends, Postdoctoral year: first, $4500.00; second, $5000.00; third, $5500.00. An additional $500.00 per year is allowed for each dependent. Those interested in joining this program should write to: Dr. Robert W. Doty, Department of Physiology, The University of Michigan, Ann Arbor, Michigan.

Societies

Midwestern section

The 12th annual scientific session of the midwestern section of the association for research in ophthalmology, was held at the Indiana University Medical Center, Indianapolis, on April 23rd and 24th. An interesting innovation was the trial of double or parallel programs. If time was left before the end of each half day, the participants in each room were permitted vote to have one or more papers from the other room represented. The program for the morning of April 23rd included: *East room:* "Electron microscopic study of early changes induced by neutron irradiation of rabbit lens and ciliary body," T. Tokunaga, E. F. Riley, and R. D. Richards, University of Iowa; "Species variation of the lens epithelium to ionizing radiation," John Dickerson, University of Iowa; "A technique for extraocular muscle electromyography in chronic animals," James A. Stuart, University of Iowa; "Thermodynamics of the intraocular and extraocular muscles," Julia Apter, Northwestern University; "Subjective evaluation of ocular proprioception monitored with the use of electro-oculograms," R. D. Reinecke, University of Kansas; "Responses and distribution of the intraocular muscles of the human eye," Julia Apter, Northwestern Univ., Chicago. *West room:* "Photic driving in amblyopia ex anopsia," James E. Miller, Laverne C. Johnson, George A. Ulett, and Margaret Johnson, Washington University; "CNS response to peripheral photic and electric stimulation in the cat," Roger S. Kirkegaard, University of Iowa; "Perceptual blinding in normal and amblyopic patients," G. K. von Noorden, and Hermann M. Burian, University of Iowa; "Permanent fractionation of the electroretinogram in glutamate poisoning," A. M. Potts, R. W. Modrell, and C. Kingsbury, University of Chicago; "Hallucinogens on retinal function in man," Alex E. Krill, University of Illinois; "The role of endothelium in corneal wound healing: Experimental study," James McDonald, University of Illinois.

On the afternoon of April 23rd: *East room:* "The role of increased responsibility in the precipitation of endogenous uveitis in adults," Evelyn Dunbar, and T. F. Schlaegel, Jr., Indiana University; "The Minnesota multiphasic personality inventory in adults with uveitis," Eugene E. Levitt, and T. F. Schlaegel, Jr., Indiana University; "The value of the Middlebrook-Dubos hemagglutination test for tuberculosis when run on aqueous samples of eyes with granulomatous iridocyclitis," T. F. Schlaegel, Jr., et al., Indiana University; "Fluorescein tagged antibody technique as an aid in diagnosis of viral ocular infections," R. Sexton, University of Iowa; "Phagocytic elements in the eye," Johannes Rohen, Washington University. *West room:* "The oculometer nerve anatomy, physiopathology and clinical lesions," James P. Rigg, and R. W. Rigg, Grand Junction, Colorado; "Studies on the subretinal fluid: I. Electrophoretic analysis," R. C. Watske, University of Iowa; "Comparative enzymology of lenticular peptidases," Renuka Banerjee, David Shoch, and E. Albert Zeller, Northwestern University; "Influence of fixatives and autolysis on the structure of the crystalline lens," R. G. Janes, and R. Richards, University of Iowa; "Experimental retinitis proliferans in rabbits produced after intravitreal injection of autoblood of saccharated iron oxide," Paul A. Cibis, and Tsuyoshi Yamashita, Washington University.

On the morning of April 24th: *East room:* "Histologic and clinical studies of the glaucoma secondary to retained intraocular iron foreign body," Tsuyoshi Yamashita, Bernard Becker, and Glen Johnston, Washington University; "Flicker fusion and luminosity functions in dichromasy," Gordon G. Heath, Indiana University; "Size effects in simultaneous color contrasts," Ingeborg Schmidt, and P. E. Grush, Indiana University; "Spectral location of subjective color purity," M. L. Rubin, University of Iowa; "Cholinergic and adrenergic compounds on rabbit zonule and ligament of Wieger," Maurice Kadin, University of Chicago.

West room: "Effect of coralox on the eye and other tissues," Maurice Kadin, University of Chicago; "Experimental tonography: The effect of anticholinesterases," Marguerite Constant, and Bernard Becker, Washington University; "The localization of Diamox-S[35] in the eye of the rabbit," Seymour B. Goren, and Frank W. Newell, University of Chicago; "Tonographic findings in relatives of glaucoma patients," Allan E. Kolker, F. Dale Roth, and Bernard Becker, Washington University; "A method of photographing fluorescence in the retinal vasculature," David Alvis and Harold Norotny, Indiana University.

Carolinas meeting

Final arrangements have been made of the joint annual meeting of the North Carolina Eye, Ear, Nose, and Throat Society and the South Carolina Society of Ophthalmology and Otolaryngology at the King Cotton Hotel in Greensboro, North Carolina, on September 12th, 13th, and 14th. The following guest speakers will be on the program: Dr. Frank Walsh, Baltimore; Dr. Howard Naquin, Baltimore; Dr. Joseph Haas, Chicago; Dr. Sam Sanders, Memphis; Dr. Philip Meltzer, Boston; and Mr. Aron Saunders, Durham, North Carolina.

For further information contact Dr. John Gordon, 412 North Church Street, Charlotte 2, North Caro-

lina, or Dr. Roderick Macdonald, 330 East Main Street, Rock Hill, South Carolina.

Pacific coast meeting

The Pacific Coast Oto-Ophthalmological Society will hold its annual meeting at the Hotel St. Francis, San Francisco, May 22nd to 26th. The following invited guest speakers will participate in the program: E. S. Perkins, London; A. M. Ostfeld, Chicago; Edwin J. Wylie, San Francisco; Bruce N. Kvernland, Portland; Jerome A. Hilger, Saint Paul; Merle Lawrence, Ann Arbor, Michigan; John R. Lindsay, Chicago; Jack V. D. Hough, Oklahoma City.

Room reservations for the meeting may be obtained by writing Mrs. Lorraine Berry, Housing Bureau, Room 300, 61 Grove Street, San Francisco, California.

Brooklyn program

Dr. R. M. Fasanella, Yale Medical College, discussed "Complications of cataract surgery," at the 156th regular meeting of the Brooklyn Ophthalmological Society.

Colorado Ophthalmological Society

Recent programs of the Colorado Ophthalmological Society in Denver have included the following guest lecturers and topics: Dr. John W. Henderson, Rochester, Minnesota, "Orbital tumors and Hemangiomas"; Dr. Paul Wetzig, Colorado Springs, "Experience with light coagulation in the treatment of retinal lesions"; Dr. Lorenz E. Zimmerman, Armed Forces Institute of Pathology, Washington, D.C., "Pathology of certain corneal dystrophies" and "Granulomatous uveitis and related diseases"; Dr. Frederick C. Blodi, Iowa City, "Heterochromia of the iris" and "Complications of ocular wound healing."

Personal

Dr. C. Dwight Townes and Dr. Arthur H. Keeney, Louisville, Kentucky, have visited Rio de Janeiro, São Paulo, Montevideo, Buenos Aires, Santiago, Lima and Bogota as guests of the Pan-American Association of Ophthalmology for the Moacyr Alvaro Lectureship, visiting universities and lecturing before ophthalmological societies. In the future this lectureship will be know as the Alvaro Lectureship of the Pan-American Association of Ophthalmology.

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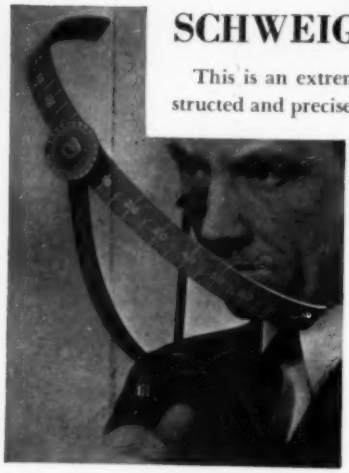

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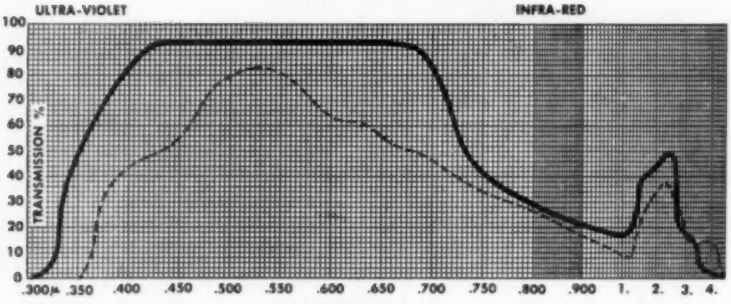

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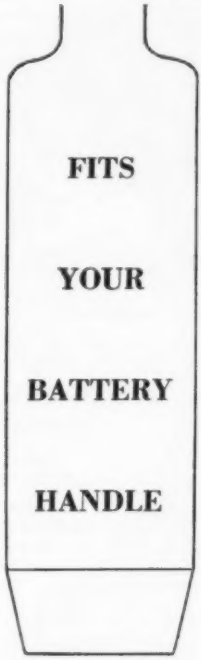

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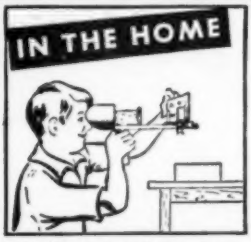

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